1988 ANNUAL REPORT

MANITOBA CANCER TREATMENT
AND RESEARCH FOUNDATION
BUILDING • CAMPAIGN

The Manitoba Cancer Treatment and Research Foundation

Annual Report for the Year 1988

90-05285/

1988 ANNUAL REPORT

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100 Olivia Street, Winnipeg, Manitoba, R3E 0V9, Telephone: 787-2241.

Cover Design and Publication: Printing Services, Communication Systems,
The University of Manitoba.

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D. J. McMullin, Esq.,
Chairman
The Manitoba Cancer Treatment
and Research Foundation

Sir:

It is my pleasure to submit the Annual Report of the Manitoba Cancer Treatment and Research Foundation for 1988. The report documents the activities of patient care, support services, educational programs and research. The supplement to the body of the report contains the cancer incidence and mortality statistics for the Province for the year.

I would like to express my personal thanks to the members of the Board who retired in 1988 and to welcome the newcomers to the Foundation. The dedication of your Board to the purposes of the Foundation guarantees the continuing commitment of the Foundation to the highest level of cancer care for this Province. It is also my sincere pleasure to acknowledge the support of the staff whose dedication makes possible the work and purpose of this Foundation.

Respectfully submitted,

L. G. Israels, M.D.
Executive Director

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

BOARD OF DIRECTORS

D. J. McMullin, *Chairman* (effective July 13, 1988)
W. D. MacDiarmid, *Chairman* (to June 30, 1988)
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Ex Officio

The Honourable W. Parasiuk (to March 1988)
The Honourable D. W. Orchard (effective May 1988), *Minister of Health*
J. Foerster, M.D., *Chairman, Advisory Medical Board*

EXECUTIVE/FINANCE COMMITTEE

(to June 30, 1988)

W. D. MacDiarmid, M.D., *Chairman*
D. McMullin, *Vice-Chairman*
A. Bishop, M.D.

EXECUTIVE/FINANCE COMMITTEE

Effective June 13, 1988

Mr. G. Horne, *Chairman*
Mr. B. Adams
Mr. L. Crane
Mr. D. McMullin

ADVISORY MEDICAL BOARD

J. Foerster, M.D., B.Sc., (Med), *Chairman*
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G. V. Krepart, B.Sc., M.D., F.R.C.S. (C), B.C.A.M. (Ob/Gyn), F.G.O., S.B.C.G.O.
L. G. Israels, B.A., M.D., M.Sc., F.R.C.P.(C)
K. Malaker, M.B., B.Sc., L.R.C.P., M.R.C.S., D.M.R.T.
I. C. Peever, M.D., F.A.C.O.G., F.S.O.G.O., F.R.C.S. (C)
B. Weinerman, M.D., F.R.C.P. (C).

SCIENTIFIC ADVISORY COMMITTEE

H. Duckworth, B.Sc., Ph.D.
Professor, Dept. of Chemistry
University of Manitoba

A. Froese, B.Sc., Ph.D.
Professor, Dept. of Immunology
University of Manitoba

F. Labella, B.A., M.A., Ph.D.
Professor, Dept. of Pharmacology and Therapeutics
University of Manitoba

Ex Officio
L. G. Israels, M.D.
Executive Director
Manitoba Cancer Treatment & Research Foundation

MANITOBA INSTITUTE OF CELL BIOLOGY BOARD OF MANAGEMENT

R. Andison, *Chairman*
N. Anthonisen, M.D. (effective July 1, 1988)
S. Berney
R. Best (effective April 1988)
A. Bishop, M.D. (effective August 23, 1988)
M. Vaisey-Genser
G. J. Goldenberg, M.D. (to June 30, 1988) — *Ex Officio*
A. Greenberg, M.D. (effective November 1, 1988) — *Ex Officio*
Mr. Justice G. Hall
L. G. Israels, M.D.
J. Jamieson, Ph.D.
D. Jessiman (to April 1988)
W. D. MacDiarmid, M.D. (to June 30, 1988)
D. J. McMullin
V. E. Nelson (to April 1988)
J. Wade, M.D. (to June 30, 1988)

ADMINISTRATION

Executive Director — L. G. Israels, M.D.
Assistant Executive Director — R. R. Publow
Executive Secretary — J. Singer, J. Morton
Administrative Assistant Finance — I. Birse
Administrative Assistant Personnel — D. Lamontagne
Accounts Payable — M. Gemmell

PROFESSIONAL STAFF

The Foundation is an integral part of the teaching and research program of the University of Manitoba. Various staff members participate in the undergraduate oncology program, teach on the hospital wards, and have graduate students in their laboratories.

UNIVERSITY APPOINTMENTS

Faculty of Medicine

- Department of Anatomy
  - Dr. G. Froese, *Associate Professor*
- Department of Biochemistry
  - Dr. J. Wright, *Professor*
  - Dr. L. G. Israels, *Adjunct Professor*
- Department of Immunology
  - Dr. F. Paraskevas, *Professor*
  - Dr. A. Greenberg, *Associate Professor*
  - Dr. D. A. Chow, *Assistant Professor*
- Department of Internal Medicine
  - Dr. L. G. Israels, *Distinguished Professor*
  - Dr. E. Baral, *Professor*
  - Dr. D. Bowman, *Professor*
  - Dr. G. J. Goldenberg, *Professor*
  - Dr. F. Paraskevas, *Professor*
  - Dr. B. Schacter, *Professor*
  - Dr. B. Weinerman, *Professor*
  - Dr. L. Brandes, *Associate Professor*
  - Dr. M. Levitt, *Associate Professor*
  - Dr. H. Schipper, *Associate Professor*
  - Dr. A. Begleiter, *Assistant Professor*
  - Dr. E. Bow, *Assistant Professor*
  - Dr. J. Johnston, *Assistant Professor*
  - Dr. H. Y. P. Lam, *Assistant Professor*
  - Dr. S. T. Lee, *Assistant Professor*
  - Dr. T. Shore, *Assistant Professor*
  - Dr. J. Wright, *Adjunct Professor*
- Department of Obstetrics and Gynaecology
  - Dr. G. V. Krepart, *Professor*
  - Dr. R. J. Lotocki, *Assistant Professor*

Department of Pediatrics
  Dr. A. Bishop, *Professor*
  Dr. A. H. Greenberg, *Professor*
  Dr. J. M. Gerrard, *Associate Professor*
  Dr. E. D. Israels, *Associate Professor*
  Dr. M. Schroeder, *Associate Professor*
  Dr. S. J. Israels, *Assistant Professor*
  Dr. N. Kobrinsky, *Assistant Professor*
Department of Physiology
  Dr. J. Dodd, *Assistant Professor*
  Dr. M. Mowat, *Assistant Professor*
Department of Radiology
  Dr. E. Baral, *Professor*
  Dr. K. Malaker, *Associate Professor*
  Dr. S. Shalev, *Associate Professor*
  Dr. P. Dunscombe, *Assistant Professor*
  Dr. G. Froese, *Assistant Professor*
  Dr. P. Hahn, *Assistant Professor*
  Dr. W. Huda, *Assistant Professor*
  Dr. K. D. Jones, *Assistant Professor*
  Dr. W. McLellan, *Assistant Professor*
  Dr. R. F. Palser, *Assistant Professor*
  Dr. A. Sourkes, *Assistant Professor*
  Dr. E. Hadzic, *Lecturer*
Department of Surgery
  Dr. E. Ramsey, *Professor*
  Dr. B. J. Anderson, *Assistant Professor*
  Dr. W. Beecroft, *Associate Professor*
Department of Social and Preventive Medicine
  Dr. N. W. Choi, *Professor*
  Dr. N. A. Nelson, *Associate Professor*
  Mrs. P. F. Moodie, *Lecturer*

Faculty of Science
Department of Microbiology
  Dr. J. Wright, *Professor*
Department of Physics
  Dr. P. Dunscombe,*Adjunct Professor*
  Dr. G. Froese, *Adjunct Professor*
  Dr. W. Huda, *Adjunct Professor*
  Dr. R. Palser, *Adjunct Professor*
  Dr. G. Sandison, *Adjunct Professor*
  Dr. S. Shalev, *Adjunct Professor*
Computer Science
  Dr. M. Laucht, *Associate Professor*

RADIATION ONCOLOGY

Acting Director — E. Baral, M.D., Ph.D.

RADIATION ONCOLOGISTS:

E. Hadzic, M.D., F.R.C.P.(C)
P. Hahn, M.D., Ph.D.
K. D. Jones, M.B., B.Ch., F.R.C.S.(Eng.), F.R.C.R.
K. Malaker, M.D., Ph.D.
W. McLellan, M.B., Ch.B., D.M.R.T., F.R.C.P.(C)
K. Vijayaraghavan, M.B., B.S.

Fellow

A. Bains, M.D.

Residents

P. A. Blood, B.M., B.Sc., T. Corbett, M.D.

Associate Member

A. Petkau, M.Sc., M.D.

Department Secretaries

S. Burgess, C. Campbell

THERAPY EQUIPMENT

M. R. MacCharles Unit:

Therac 40 Sagittaire linear accelerator
4 MeV S.H.M. linear accelerator
A.E.C.L. Model F. Cobalt 60 beam therapy unit
250 kV x-ray therapy unit
140 kV x-ray therapy unit
Picker simulator
A.E.C.L. Therasim 750 simulator
A.E.C.L. Theraplan treatment planning computer
TAGMED 2450 MH$_z$ hyperthermia unit

St. Boniface General Hospital Unit:

100 kV superficial x-ray therapy unit
A.E.C.L. Theratron 780 Cobalt unit
Picker simulator

EXTERNAL IRRADIATION

At the M. R. MacCharles Unit, 1,243 new patients were treated and 534 patients were re-treated.

At the St. Boniface General Hospital Radiation Oncology Unit, 357 new patients were treated and 252 patients were retreated.

	M.R. MacC.	**S.B.G.H.**	**Total**
Patient visits	20,091	3,868	**23,959**
Treatments	26,459	6,660	**33,119**

NUMBER OF TREATMENTS WITH RADIOACTIVE SOURCES

Cesium 137	**Gold Grains**	**Iridium 192**	**Beta Applicator**	**Total**
94	0	21	21	136

INTRODUCTION

The Department of Radiation Oncology is a fully integrated program of the Manitoba Cancer Treatment and Research Foundation. The consultative and therapeutic services are provided at the M. R. MacCharles Unit, at which major equipment facilities are located and also at the St. Boniface Hospital Oncology Unit where an isocentric telecobalt unit and simulator facility are available. Due to the evolution and eventual expansion of the co-ordinated multispecialty oncology program including integrated radiotherapy and chemotherapy clinics at St. Boniface, the need for complete state-of-the-art radiotherapy equipment has become apparent. Following a series of constructive discussions with the government, it is now hoped that the St. Boniface Hospital Oncology Unit will be equipped with a dual energy linear accelerator and an adequate infrastructure including the presence of Medical Physics, Treatment Planning and Mould room will be provided. Once the above is implemented, two full time senior radiation oncologists will be participating in out-patient services. Generally speaking, because of the demand for more sophisticated planning of radiation therapy, and also due to the increasing number of treatments, waiting times for treatment remain a problem, particularly with respect to both available linear accelerators. As an attempt to keep the waiting times for treatment within acceptable limits, the working hours for the single high energy linear accelerator remain extended to between 7:30 a.m. and 10:30 p.m. The need for extended working hours will probably remain throughout the year 1989. The radiation therapy technologists, physicists and staff of the Department of Radiation Oncology have all generously given their time and support to bringing this difficult problem under control. We expect that the second high energy linear accelerator will be installed at the M. R. MacCharles unit of the Manitoba Cancer Foundation in June 1989 and the 4 MeV low energy linear accelerator will be replaced by a 6 MeV machine. The requirement for co-ordinated prospective patient management has already lead to the establishment of integrated multidisciplinary and site oriented clinics for breast cancer, tumors of the central nervous system, whereas lung tumor clinic will be in place by March 1989. Eventually, most of the out-patient clinics will be conjointly staffed as part of an overall integration plan. Also, the weekly head and neck multidisciplinary clinic is functioning well with attendance of clinicians from both the Health Sciences Centre and St. Boniface Hospital. The liaison between the Departments of Surgery, Internal Medicine and Diagnostic Radiology remains very close. An in-patient Radiation Oncology ward has been established in conjunction with Surgical Oncology at Health Sciences Centre where both disciplines co-operate in a very intimate manner. There is a continuing problem with a shortage of brachytherapy beds for the non-gynecology brachytherapy patients. O.R. time for brachytherapy remains insufficient and constructive discussions are currently on-going, aimed at improvement of this particular problem as soon as possible.

STAFFING

Seven Radiation Oncologists are currently on staff and Dr. Stephan Larsson from Birmingham, U.K. will be joining the Department of Radiation Oncology as a staff member in March 1989. We expect that ten senior staff positions are necessary in order to provide adequate radiation therapy services for both treatment, teaching and research.

TEACHING

The Department of Radiation Oncology has a clearly defined Specialty Training Committee which currently is in the midst of revising its educational plan. The required functions of the Residency Program Committee are carried out in an orderly fashion. The strength of the program is its clinical material which is large and varied. Many opportunities exist for interdisciplinary discussions, problem solving and teaching. Resident evaluation has been implemented and regular examinations consisting of both the written and oral parts are underway. Informal but readily available, career consulting is practiced. There are currently two residents in the program, Dr. Paul Blood who is a third year resident and Dr. Tom Corbett who is a first year resident. Commencing in July 1989, Dr. Ahmet Leylek will enter the residency training program. It is expected that the residents will become increasingly involved in research activities. The department is integrated with the University of Manitoba for both graduate and undergraduate teaching and there is an increasing involvement of the department in the teaching of second and fourth year medical students.

ACADEMIC AND SCHOLARLY ACTIVITIES

New Patient Conference weekly.
Treatment Planning Meeting every other week.
Clinical Seminar once a month.
Basic Science Seminar weekly.
Integrated Pathology/Radiology Rounds bi-weekly.
Breast Tumor Conference weekly.
Brain Tumor Conference weekly.
Tumor Pathology and Clinical Rounds at St. Boniface Hospital once a week.

RESEARCH

Basic research involves Immunology and Radiobiology whereas clinical research involves hyperthermia, different patterns of fractionation of radiation treatment, radiotherapy of carcinoma of the prostate, as well as active participation of the department in the large co-operative groups — NCIC, NSABP and RTOG.

CLINICAL INVESTIGATION

HYPERTHERMIA

Dr. K. Malaker, Dr. P. Dunscombe and Dr. G. Froese

The hyperthermia team continues to accept patients with superficial tumors on low dose radiation with hyperthermia. Schedules have now changed from five times to twice weekly hyperthermia, which is given immediately following radiation, using Tagmet 2250 MHz micro-system for superficial tumors no deeper than 3 cm. and for skin surfaces and surface extension less than 6 cm. in diameter. We continue to use a surface heating system with controlled heating pad for extensive skin involvement as a part of a phase I trial.

SUPERFRACTIONATED AND MULTIPLE DAILY FRACTIONATED RADIOTHERAPY

Dr. K. Malaker and Dr. W. McLellan

Superfractionated radiation research in the clinical setting continues to accrue patients. However, because of the acute shortage of machine time and a long waiting list, accrual in many sites has been temporarily suspended to continue at a later date when three machines are in clinical use.

CLINICAL RADIOBIOLOGIAL STUDY OF BREAST IRRADIATION

Dr. K. Malaker, M. Stewart and M. Chambers

Physical changes due tc radiation induced edema can cause changes in the depth dose and also volume of the particular site. Selected patients with carcinoma of breast are being investigated to study the changes in contour during the course of radiation and also the volume of the breast itself. Contours are taken on Day 0, Day 10 and Day 25 of the radiation treatment, and volumes measured with water displacement technique on Day 1 and Day 25. Changes in contour during the course of radiation are seen, the difference in the actual depth dose distribution and prescribed distribution are studied. Changes in the breast volume during the course of radiation are also measured and comparison is being made with the actual integral dose of irradiated breast and the prescribed integral dose with the help of the isodose distribution. Significant alterations have been noted in 30% of cases, however the biological and clinical implications of this variable will require several years of follow up.

STUDY OF MANAGEMENT DYSPLASIA/IN SITU CARCINOMA IN HEAD AND NECK CANCER UNIT

Dr. K. Malaker, Dr. B. J. Anderson and Dr. W. A. Beecroft

Patients with mucosal dysplasia of the oral cavity, oropharnyx and tongue and also carcinoma in situ are frequently referred to the multidisciplinary Head and Neck Clinic at the Manitoba Cancer Foundation. A pilot study is being carried out to evaluate beta-carotene and retinoid (Acutane) on the natural history of mucosal dysplasia and in situ carcinoma. Patients are entered in the study, having had histologically proven diagnosis, failed on topical medications, steroids, systemic medications, vitamin therapy and in some cases, surgical management. The protocol includes assessment of pretreatment level of hepatic function, serum vitamin A, beta-carotene and retinoids, clinical examination and accurate mapping of the abnormal areas followed by three-monthly clinical photography for evaluation. Beta-carotene 120 mg. per day is prescribed for three months for initial evaluation and continued for one year if response is apparent. Otherwise, switch to retinoic acid orally 10 mg. twice a day for three months for initial evaluation. So far there has been no significant toxicity noted from beta-carotene or retinoids.

REGISTRY OF DELAYED RADIATION REACTION

Dr. K. Malaker

We are continuing to register and document all patients with significant delayed radiation reaction, i.e. neuropathy, fibrosis, neuritis, etc. to study the natural history, radiation biology and clinical radiation pathological aspects of delayed radiation complications. On the satisfactory accrual in this series, following analysis, it is hoped that the findings will lead to the investigation of a genetic response to radiation reaction. Formulation of such a study is being actively discussed with the Department of Genetics.

LABORATORY INVESTIGATIONS

IN VITRO EFFECT OF ADRIAMYCIN AND MELPHALAN ON NON-PROLIFERATING AND PROLIFERATING EPITHELIAL CELLS

Dr. Edward Baral and Dr. Gert Auer, Department of Tumor Pathology, Karolinska Hospital, Stockholm, Sweden

This project studies the effects of Adriamycin and Melphalan on proliferating and non-proliferating cultured embryonal mouse kidney cells. The proliferating activity of the cells is determined by combined DNA and total nuclear protein measurements. The results demonstrate in a very convincing way the preferential effect of cytotoxic drugs on the cycling cells as compared to the non-cycling ones.

THE EFFECT OF ESTRADIOL AND TAMOXIFEN ON LYMPHOCYTE REACTIONS IN VITRO

Dr. Edward Baral and Dr. Istvan Berczi, Department of Immunology, University of Manitoba

A rapidly increasing body of experimental evidence indicates that estradiol is an important immunodulatory hormone. Estrogen antagonist drugs, such as tamoxifen, also effect the immune system as founded by these and by other investigators. The immunodulatory effects of these agents on the immune system has not been firmly established. Theoretically, several possibilities exist, of which the applicants propose to examine the direct action of estradiol and of tamoxifen on in vitro lymphocyte reactions. Human and rat lymphoid cells are used throughout. Mixed lymphocyte reactions, autologous mixed lymphocyte reactions, reactions to mitogens (PHA, PWM, and LPS) are examined. The possible effect of these agents on the production of interleukin-1 and interleuken-2 by human and rat lymphocytes are also studied. The specific aims are as follows: (i) to establish the effect of drug levels in culture using physiological and pharmacological drug concentrations. The time intervals needed for exposure of the cells and the kinetics of reactions under the influence of these agents; (ii) to study the cell types affected, e.g. whether, B, T and/or macrophage type cells are involved. Subsets of T-lymphocytes (e.g. helper-inducer type and suppressor-killer type) will also be studied from this point of view and with the aid of monoclonal antibodies; (iii) to compare the effect of estradiol and tamoxifen when applied parallel and jointly to cultures of each reaction examined in an effort to elucidate whether their effect is antagonistic or synergistic.

The significance of these studies lies with the fact that both estradiol and tamoxifen are widely used in medicine, yet their effects on the immune system are seldom taken into consideration. The information obtained from proposed experiments may not only provide new insights for the more rational use of these drugs, but also may open up the novel area of hormonal treatment of immunological disorders.

SUPEROXIDE DISMUTASE AS A PROTECTOR OF RADIATION PAROTITIS

Dr. K. Malaker and Dr. R. M. Das

Superoxide dismutase, produced by the Rh Laboratory, is being used to study the effect of the enzymes as radioprotector against radiation parotitis in Sprague-Dawley rats. The study is being conducted in groups of animals using 3000 cGy as single dose with superoxide dismutase before and after radiation and a control group of animals receiving 3000 cGy and injections of the normal saline of the same volume before and after radiation. Serum amylase is measured prior to radiation and 24 hours after treatment. The animals are sacrificed 24 hours after treatment. The parotid glands are dissected and submitted for histopathological studies to establish the differece in the nectoric index. The preliminary studies indicate significant protection by superoxide dismutase compared with the two control groups.

RADIOTHERAPY OF CANCER OF PROSTATE — COMPARISON OF CT SCAN VS CONVENTIONAL PLAN

Dr. P. Hahn, Dr. S. Shalev and Dr. N. Nelson

Clinical investigation continues in a randomized study where evaluation is being made on the difference of acute and delayed radiation reaction and tumor control in groups of stage A_2 and B carcinoma prostate patients treated for cure planned either with the help of CT scan or by standard radiologic technique.

MAGNETIC RESONANCE SPECTROSCOPY OF RADIATION REACTION OF NORMAL TISSUE

Dr. K. Malaker, Dr. R. M. Das, Dr. J. M. Peeling and Dr. W. Huda

Very limited data is available on the biochemical changes in normal tissue following irradiation. The understanding of biochemical changes at various points in time following radiation will perhaps help to understand the ways and means to interfere with the process and reduce the radiation-induced damage. Preliminary work using Sprague-Dawley rats' totally shaved skin indicated MR spectroscopy to be a viable tool for assessment of various amino acids in the specimen. Work is now in progress to evaluate by MR spectroscopy rat skin biopsied at 0 to 1/2 hour, 1, 3, 6, 9, 12, 24 and 48 hours after radiation, which will be compared to normal control unirradiated animals. The program also includes comparison of MR spectroscopy of radiation skin with surgical wound and third degree burn of rat skin produced by controlled heating. Skin biopsy will be taken at specified intervals as above. A study will also be carried out to evaluate the effect of superoxide dismutase (radio-protector) on irradiated rat skin.

PUBLICATIONS

Nylen, U., Baral, E., Svan, G. and Rutqvist, L. E. Low dose doxorubicin in the treatment of metastatic breast cancer. Acta Oncologica 1988. In press.

Malaker, K. and Das, R. M. Effect of superoxide dismutase on early radiation injury of lungs in the rat. Molecular and Cellular Biochemistry, **84**: 141-145, 1988.

Malaker, K. and Das, R. M. The effect of superoxide dismutase on the pathogenesis of radiation-induced pulmonary damage in the rat. Therapeutic Pharmacology, **39**: 327-330, 1988.

Shalev, S., Bartel, P., Therrien, P., Hahn, P., Carey, M. The objective evaluation of alternative treatment plans: Images of regret. Int. J. Rad. Oncol. Biol. Phys., **15**, 763-767, 1988.

MEDICAL ONCOLOGY* (M. R. McCharles Unit)

Director — David M. Bowman, M.D., B.Sc.(Med), FRCPC

MEDICAL ONCOLOGISTS

L. Brandes, M.D., B.Sc.(Med), FRCPC
J. Foerster, M.D., B.Sc.(Med)
G. Goldenberg, M.D., Ph.D., FRCPC
L. G. Israels, B.A., M.D., M.Sc., FRCPC
J. Johnston, M.B., FRCPC
M. Levitt, M.D., M.Sc., FRCPC
B. Schacter, M.D., B.Sc.(Med), FRCPC

CLINICAL FELLOWS

B. Zanke, M.D., FRCPC

RESIDENTS

J. Canvin, M.D., E. Carlisle, M.D., R. Cartagena, M.D., S. Choudri, M.D., D. Duerksen, M.D., J. Dupont, M.D., D. Houston, M.D., W. Leslie, M.D., S. Marantz, M.D., D. McDonald, M.D., D. Remis, M.D., C. Stern, M.D., H. Wrinkler, M.D.

NURSING STAFF

N. Johnson (Senior Chemotherapy Nurse)

Clinical Nurses

S. Borrett, S. Bracken, J. Cherland, I. Chrynuk, L. Friesen, E. Nelson, D. Rumpel, S. Switzer

Nursing Aides

I. De Sousa, L. Jonasson, U. Merck, C. Jones

CLINICAL INVESTIGATION OFFICE

Director — M. Levitt, M.D., M.Sc., FRCPC
Senior Protocol Nurse: K. McDonald, R.N.
Protocol Nurse: V. Powell, R.N.

Protocol Technicians

Senior Technician: E. Stiles
K. Hjalmarsson-Taylor, H. Kampen, L. Love, M. Parisien.

Clinic Receptionist

C. Jones, M. Powder

Departmental Secretaries

S. Ireland, J. Powell, T. Reutcky

ORGANIZATION

The Manitoba Cancer Treatment and Research Foundation Department of Medical Oncology provides programmes for diagnosis and management of adults with neoplastic and hematologic diseases in Manitoba. Patients are also referred from neighbouring provinces and states. Facilities are maintained geographically at the Foundation and at St. Boniface General Hospital (See also report of "Oncology Unit — St. Boniface General Hospital"). The Foundation also coordinates a Cancer Outreach Programme to provide rural patients and their families with optimal standards of care close to their home environment. All Medical Staff have full-time appointments at the University of Manitoba and most are actively conducting programmes of basic research and/or clinical investigation.

The Oncology Centre at the Foundation is an Outpatient facility also housing the research programmes of the Manitoba Institute of Cell Biology, such that basic research, clinical investigation and patient care programmes are intimately related. The Department of Medical Oncology includes eight medical oncologists, who provide care for patients with malignant and hematologic diseases. In addition, close liaisons with radiation oncology, gynecological, urological and surgical oncology, plus pediatric oncology are maintained. The professional team includes oncology nurses specialized in parenteral administration of chemotherapy and immunotherapy. The Radiation Oncology service is also located within the Oncology Centre, thus, facilitating interdisciplinary approaches to cancer care. A hematology laboratory at the Oncology Centre provides hematologic data of high quality promptly and efficiently to all of the clinics as is essential to the ongoing care of both urban and rural patients. Other patient services in the Oncology Centre include a special cancer-oriented Social Service, and Epidemiology and Statistics Section. These outpatient services are integrated with the inpatient services of the adjacent Health Sciences Centre. Thus, when necessary, patients are admitted to the clinical teaching units of the General Centre (HSC). Here they are cared for by the House Officers and the Oncology Fellows under the supervision of the senior consultant of the Medical Oncology Service. The Medical Oncology Service also provides the Hematology/Oncology consulting service to inpatients of the Health Sciences Centre.

TEACHING

In addition to the service component involved in care of ambulatory patients with neoplastic disease, the Medical Oncology Service provides teaching for students at an Undergraduate level through lectures in Hematology and Oncology, and a laboratory hematology course; and at the graduate level of Interns and Residents in the Department of Medicine. Full-time Clinical Fellows and Residents in Internal Medicine rotate on the Hematology/Oncology Service, both at the Health Sciences Centre and St. Boniface Hospital. In addition, they participate in the Clinical and Research Seminars and Rounds of the Department as well as Resident Basic Science Seminars and weekly "Walkarounds" with senior staff emphasizing both clinical-morphological findings and disease management. All third year undergraduate medical students at the University of Manitoba are given a series of Hematology case reviews under the supervision of various members of the Attending Staff and the Hematology Fellows. Some of the fourth year medical students also participated in one-month selectives on the Hematology/ Oncology Service. The Hematology/Oncology Morphology Teaching Laboratory under the direction of Ms. A. Sasyniuk, R.T., B.Sc., participates fully with the Medical Oncology Department including the St. Boniface Hospital Unit, in the teaching of Medical and Pediatric fellows and rotating residents, as well as the fourth year clerks and third year clerks participating in the Hematology/Oncology electives.

The purpose of this laboratory is to:

1. Coordinate the clinical teaching with the laboratory data.
2. Train fellows, residents and clinical clerks in the Hematology/Oncology programme to interpret the morphology of the peripheral blood and bone marrows obtained from patients they have seen in clinic or admitted to hospital.
3. Give each clinical clerk during their elective, a caseload of patients, representative of the spectrum of ages in normal and disease states. Therefore, providing students with experience to develop efficiency in obtaining relevant history, to recognize life threatening problems and to establish priorities in management in acute and chronic situations.

The schedule provides 4-6 hours/week training in examination of morphology and interpretation of peripheral blood smears, bone marrows and biopsies on a one to one basis. Each student has the opportunity to examine the above material at the time of diagnosis, during treatment, and during remission.

For those who choose to rotate through this program the major emphasis of this laboratory is to integrate and to broaden the understanding in Hematology/Oncology. It also provides an opportunity to gain first hand experience at interpretation of peripheral blood smears and bone marrow smears and a fuller utilization of useful diagnostic tests.

The Excellent teaching in the laboratory is provided by Ann Sasyniuk, assisted by Betty Jacobucci. The program is an important complementary experience for physicians in pediatric pathology and internal medicine.

During 1988, visiting guest speakers included Dr. Martin Palmer (University of Alberta) speaking on "Clinical Trials in Multiple Myeloma", Dr. Joe R. Bertino (Memorial Sloan Kettering Cancer Centre) speaking on "Protection of Bone Marrow from Toxicity by Transfection with Drug Resistant Genes"; Dr. Robert Buckman (Univeristy of Toronto) whose topic was "I don't Know What to Say — How to Help and Support Someone Who is Dying", and Dr. Stan Riddell (University of Washington, Fred Hutchinson Cancer Centre) speaking on "Bone Marrow Transplantation" and "Immunology of Cytomegalovirus Infection".

BASIC RESEARCH

The clinical facility on the ground floor of the Oncology Centre is intimately juxtaposed with the Manitoba Institute of Cell Biology, which is situated on the second floor of the same building. This relationship allows sophisticated tests and expert consultations to be immediately available from laboratories doing research in tumor immunology, blood coagulation, molecular biology, and membrane transport of chemotherapeutic agents. Please see the separate report of the Manitoba Institute of Cell Biology for descriptive details and the appended publication citations.

CLINICAL INVESTIGATION

New developments in medical therapy of cancer have made the conduct of a clinical investigation programme the cornerstone of developing cancer treatment programmes. In Medical Oncology, programmes of clinical investigation are carried out, both on an independent basis, and in collaboration with major clinical trial co-operative groups.

The Protocol Review Committee, with multidisciplinary membership evaluates and approves all new clinical protocols involving the Manitoba Cancer Treatment and Research Foundation patients. Committee membership includes Drs. M. Levitt (Chairman), D. Bowman, B. Weinerman, K. Malaker, G. Krepart, N. Kobrinsky, and L. G. Israels.

The Department of Medical Oncology also participates in clinical trials sponsored by several national and international clinical trial co-operative groups, including the National Cancer Institute of Canada (NCIC — Principal Investigator — Dr. M. Levitt), and the National Surgical Programme for Breast and Bowel Cancers (NSABP — Principal Investigator, Dr. D. M. Bowman). Participation in numerous protocols with these co-operative groups and institutions remains a high priority of medical oncology. We believe these multi-institutional co-operative trials represent the forefront of developmental cancer therapeutics.

Table I, which follows, indicates our participation in these protocols during recent years.

SUMMARY OF 1988 STATISTICS

TABLE I

CLINICAL INVESTIGATIVE PROTOCOL ACCRUAL — ADULT

Study Group:	**1987**	**1988**
NCIC		
Remaining On-Study from Prior Years	351	312
New Patient Accrual	22	17
Off Study	61	22
Remaining On-Study	312	307
NSABP		
Remaining On-Study from Prior Years	374	386
New Patient Accrual	30	33
Off Study	18	23
Remaining On-Study	386	396
RTOG (New Institution — Affiliate Member as of July 1988)		
Remaining On-Study From Prior Years	—	—
New Patient Accrual	—	11
Off Study	—	0
Remaining On-Study	—	11
LOCAL TRIALS		
Remaining On-Study from Prior Years	98	107
New Patient Accrual	43	12
Off Study	34	32
Remaining On-Study	107	87
TOTAL ON-STUDY (Year End)	**805**	**801**

Table II, following, provides a brief description of active clinical investigative trials for adult patients in 1988.

TABLE II

Disease Site	Protocol Number	Brief Description
Ovarian Carcinoma	NCIC OV.6	Non-randomized study to determine the efficacy of surgery alone in patients with Stage IA or Stage IB disease when extensive surgical staging has also been done to confirm limited disease.
	NCIC OV.7	To compare current optimum chemotherapy with abdominopelvic irradiation in Stage IC, IIA, B, C, or III, with microscopic disease. 1. RT to abdomen x 22 treatments and RT to pelvis x 11 treatments VERSUS 2. Cyclophosphamide I.V. and Cis-Platinum I.V. q 4 weeks x 9 courses.
	NCIC OV.8	To compare Carbo-platin plus Cyclophosphamide in patients with macroscopic residual disease. Responders receive whole abdominal irradiation.
Lung Carcinoma	NCIC BR.6	To compare early versus late radiotherapy in limited small cell carcinoma for patients being treated with Cyclophosphamide I.V., Adriamycin I.V., Vincristine I.V., Cycles 1,3,5, alternating with VP-16 I.V. Cis-platinum I.V. daily x 3 days cycles 2,4,6.
	NCIC BR.7	Pilot Study — Single arm Phase II trial to determine if concomitant hyperfractionated radiotherapy and alternating non-cross resistant chemotherapy is a tolerable treatment in limited small cell carcinoma of the lung.
	MBR 86.1	A randomized study to compare the toxicity and effectiveness of radiotherapy plus lonidamine with "standard" radiotherapy itself in patients with inoperable cell lung cancers without distant metastases.
	MMT 86.3	To determine the response rate to Epirubicin administered at escalating doses as an I.V. bolus, every 3 weeks in patients with malignant pleural and/or peritoneal mesothelioma.

	MBR 88.1	CARBO-CIS II — Study of Carboplatin and Cisplatin in combination with etoposide in previously untreated, small cell lung cancer and in combination wiuth etoposide and bleomycin in previously untreated non-resectable non-small cell lung cancer.
Lymphoma	NCIC LY.3	Comparison of Standard BACOP chemotherapy with escalated BACOP in "poor prognosis" histology.
Leukemia	NCIC HL.1	A randomized comparison of Deoxycoformycin vs. Alpha-Interferon in previously untreatment patients with Hairy Cell Leukemia.
	MLK 88.2	Resistance to alkylating agents in chronic lymphocytic leukemia.
Bone Marrow	MBM	Phase I - II Trial of Thalidomide with or without cyclosporine in the treatment of refractory chronic graft-versus-host disease (GVHD).
Hodgkin's Disease	NCIC HD.4	To study the effectiveness of MOPP/ABV Hybrid chemotherapy versus alternating MOPP/ABVD for remission induction, durability and survival in advanced or recurrent disease.
Multiple Myeloma	N.MY 84.1	Pilot study of weekly Cyclophosphamide and alternate Prednisone therapy (CWAP) as primary treatment in multiple myeloma, Stages I - IV.
Malignant Melanoma	NCIC ME.5	Surgical study to determine the safest excision margins around the primary melanoma and to evaluate the management of the regional lymph nodes. A national intergroup protocol.
Colorectal Carcinoma	NSABP C-02	To evaluate postoperative portal vein infusion of 5-FU in resectable adenocarcinoma of colon.
	NSABP CO-3	A clinical trial to compare adjuvant leucovorin and 5-FU (LV-5-FU) with adjuvant MeCCNU, Vincristine and 5-FU (MOF) in patients with Dukes' B and C carcinoma of the colon.
	NSABP	A clinical trial to compare adjuvant MethylCCNU, Vincristine, 5-FU (MOF) with and without radiation in patients with Dukes' B and C carcinoma of the rectum. (Females are excluded from this study).
	NCIC CO.2	To determine the response rate and survival of patients with metastatic colorectal cancer using 5-FU continuous systemic infusion x 14 days q28 days, vs. 5-FU I.V. bolus x 5 days q28 days.

	NCIC CO.3	To determine whether adjuvant treatment with 5-FU and folinic acid versus control is effective in increasing survivorship and prolonging the disease free interval in patients undergoing curative resection of colonic adenocarcinoma.
	MCR 85.9	To determine the efficacy and toxicity of Methotrexate and 5-FU (with leucovorin rescue) in patients with advanced colon and rectal carcinoma.
Breast Carcinoma	NCIC MA.4	To compare Tamoxifen vs. Tamoxifen plus combination chemotherapy in patients with ER or PR positive stage II breast carcinoma.
	NSABP B-13	To compare no treatment versus combination chemotherapy in patients with ER and PR negative stage I breast carcinoma.
	NSABP B-14	To compare placebo versus Tamoxifen in patients with ER and PR positive stage I breast carcinoma.
	NSABP B-15	Clinical Trial comparing Adriamycin-Cyclophosphamide with or without interval re-induction Cyclophosphamide, 5-FU and Methotrexate in Stage II breast cancer patients.
	NSABP B-16	A clinical trial comparing Tamoxifen alone vs. L-PAM, 5-FU & Adriamycin & Tamoxifen or vs. Short Intensive Adriamycin-Cyclophosphamide & Tamoxifen in positive nodes patients.
	NSABP B-17	Randomized study to evaluate post operative breast irradiation following segmental mastectomy plus axillary dissection in patients with non-invasive intraductal adenocarcinoma.
	M.B. 86.4	Randomized parallel comparison of two regimens as first-line chemotherapy for advanced breast cancer — Cyclophosphamide, Novatrone and 5-FU vs. Cyclophosphamide, Adriamycin and 5-FU in advanced breast cancer.
	M.B. 88.3	Epirubicin high dose vs. conventional dose in metastatic breast cancer. A randomized study in women after CMF failure.
Prostate Carcinoma	PR 86.2	To determine whether Epirubicin, given as an intravenous injection q3 weeks, produces responses in patients with hormone resistant prostatic carcinoma with measurable disease.
	PR 84.1	Ph. III randomized Megestrol Acetate plus low dose stilbestrol vs. Diethylstilbestrol in Stage D2 prostate cancer.

	PR 88.4	A comparison of Flutamide capsules vs. Flutamide tablets in previously untreated prostate cancer patients.
	RTOG 85-31	Phase III study of Zoladex adjuvant to Radiotherapy in unfavorable prognosis carcinoma of the prostate.
	RTOG 86-10	Phase III study of Zoladex and Flutamide used as cytoreductive agents in locally advanced carcinoma of the prostate treated with definitive radiotherapy.
Bladder Carcinoma	BL 85.10	To evaluate in a randomized, double-blind trial, the efficacy of INTRON A in patients with superficial bladder cancer — specifically carcinoma-in-situ.
	NCIC BL.3	To determine whether the addition of concomitant Cis-platin to pre-operative or radical radiotherapy in patients with advanced transitional cell carcinoma of urinary bladder results in: increased incidence of clinical and pathological downstaging, improved local control, reduced incidence of metastases, increased survival and possible complications of treatment regimens.
Renal Carcinoma	NCIC IND.38	Phase II study of recombinant Tumor Necrosis Factor in metastatic renal cell carcinoma.
Metastatic Carcinoma	M.CA 85.8	To determine primarily toxicity, and secondly effectiveness, of Lonidamine plus Interferon in metastatic carcinoma patients for whom there is no effective conventional treatment.
Supportive Care	M.SC 85.7	To determine the effectivenss of Piroxicam added Morphine as an analgesic in cancer patients.
Symptom Control	NCIC SC.4	Double-blind assessment of the antiemetic efficacy, tolerance and safety of BRL 43694A in comparison with high dose metoclopramide dexamethasone and diphenhydramine in patients receiving highly emetogenic cisplatin chemotherapy.
	NCIC SC.5	Double-blind assessment of the antimetic efficacy, tolerance and safety of BRL 43694A in comparison with dexamethasone and prochlorperazine in patients receiving moderately emetogenic chemotherapy.
Staff Related Studies	NSABP	Health and Occupational Exposure to Anticancer Drugs.

MEDICAL ONCOLOGY NURSING

Medical Oncology Nursing at the Foundation continues under the leadership of Nancy Johnson in the Chemotherapy Clinic with a staff of eight chemotherapy nurses and four nursing aides devoted to the education, support, and particularly expert administration of parenteral chemotherapy for their patients. Protocol Nurse, Kerry McDonald now provides the nursing co-ordination between Medical Oncology clinics and the Clinical Investigation Office.

Regular Nursing Conjoint Rounds with Social Service have been beneficial in identifying high risk situations and intervening with appropriate measures to prevent crisis development. Increasing awareness of the role of the Oncology nurse by the University of Manitoba and Health Sciences Centre Schools of Nursing has been evidenced by placement of senior nursing students at the Foundation as part of their clinical experience. Education in the wider community continues to be encouraged and the medical oncology nurses' lecture programmes continue to attract nursing attendance from throughout the province. The nursing staff also frequently act as guest speakers at other urban and rural health institutions. Continued participation in national and international oncology meetings enhances skillful evaluation and counselling for patients and their families.

Our two nurse oncologists who completed the Faculty of Medicine second year undergraduate programme in physical diagnosis previously are proficient in assisting medical oncologists in clinical evaluation of patients at the Oncology Centre. In addition, they provide a critical liaison between patient care in the clinic and clinical investigation (protocol) activities including evaluation of patients with respect to eligibility, informed consent, and on-going assessment during therapeutic trials.

Nursing research is fostered in conjunction with the University of Manitoba School of Nursing, and with National Cancer Institute, National Surgical Adjuvant Breast and Bowel Programme, as well as institutional protocols.

A Hemophilia Clinic now operates from the Foundation, co-ordinating adult hemophilia care.

Nursing members are actively participating on a provincial committee with the Manitoba Association of Registered Nurses in developing comprehensive standards for the emerging specialty of Oncology Nursing.

PATIENT CARE

Optimal patient care remains the primary objective of the Department of Medical Oncology. The Medical Oncology Clinic, in conjunction with the unit at St. Boniface Hospital, serves as the Manitoba referral centre for care of patients with neoplastic and hematologic diseases. The adult clinic also operates in close co-operation with active pediatric oncology clinics, which are reported in detail elsewhere in this Report. While the clinic itself is strictly an ambulatory (outpatient) facility, all attending oncologists hold major University of Manitoba appointments and are on active staff at the contiguously adjacent General Centre of the Health Sciences Centre. Accordingly, patients requiring admission to Hospital are admitted to the General Centre, where they are attended in continuity by their medical oncologist.

Table III illustrates the ambulatory (out-patient) services. (See also separate report for St. Boniface Hospital Unit).

TABLE III
MEDICAL ONCOLOGY PATIENT STATISTICS#

	New Patients#	Follow-up Visits	Total Physician Clinic Visits
1983	293	5107	5400
1984	287	5125	5412
1985	291	5313	5604
1986	286	5578	5864
1987	221	5268	5489
1988	407	6371	6778

#These figures do not include approximately 500 consultations provided by Department members annually to in-patients located at the Health Sciences Centre.

IN-PATIENT (HEALTH SCIENCES CENTRE) MEDICAL ONCOLOGY

After more than a decade of planning, and with primary impetus from the Manitoba Cancer Treatment and Research Foundation, including its Executive Director and Board, during 1988 ward D6 of the Health Sciences Centre was extensively renovated including a major hi-efficiency particle air filtration system to provide an appropriate protected environment for immunocompromised, granulocytopenic patients undergoing intensive chemotherapy.

Opening ceremonies and dedication of the D6 Oncology Unit were held September 15th, 1988, conducted on the Unit by Dr. David Bowman with dedication addresses by the Honourable Dr. George Johnson, Lieutenant-Governor of Manitoba, the Honourable Don Orchard, Minister of Health and Social Services, Mr. John Bulman, Chairman of the Board, Health Sciences Centre, Mr. Dennis McMullin, Chairman of the Board, Manitoba Cancer Treatment and Research Foundation, Dr. Arnold Naimark, President, University of Manitoba, and Dr. Lyonel Israels, Distinguished Professor of Medicine (University of Manitoba) and Executive Director, Manitoba Cancer Treatment and Research Foundation.

The Honourable Dr. George Johnson, The Honourable Don Orchard and Ms. Laurie Watts, representing our patients, "cut the ribbon" collectively and declared the Unit open at 2:20 p.m., beginning a new era of patient care at the Health Sciences Centre in cooperation with the Manitoba Cancer Foundation.

SCIENTIFIC BASIS OF MEDICINE AND FESTSCHRIFT (1988)

In conjunction with the D6 Oncology Unit dedication and opening (see above), a Scientific Basis of Medicine Symposium was held September 15-16, ably coordinated by Dr. Martin Levitt, honoring Dr. Lyonel G. Israels, Distinguished Professor of Medicine, and Section Head of Hematology-Oncology at the University of Manitoba from 1960-1987. On September 15th, speakers included Dr. D. Bergsagel (Princess Margaret Hospital and University of Toronto) "Dr. Lyonel G. Israels — Impression of a Colleague", Dr. J. Foerster (University of Manitoba) "Cancer Research Development — Winnipeg", Dr. L. Siminovitch (Mount Sinai Hospital and University of Toronto) "Cancer Research and Development — Canada", and Dr. J. Bertino (Memorial Sloan Kettering Cancer Centre) "Cancer Research and Development — USA".

Further scientific papers of the symposium Friday, September 16th included: Dr. G. Goldenberg (University of Manitoba) — "Resistance to Adriamycin in Cell Lines".

Dr. J. Johnston (University of Manitoba) — "Resistance to Alkylating Agents in Leukemia".

Dr. J. Bertino (Sloan Kettering Cancer Centre) — "Detection of Resistance in Patient Biopsies".

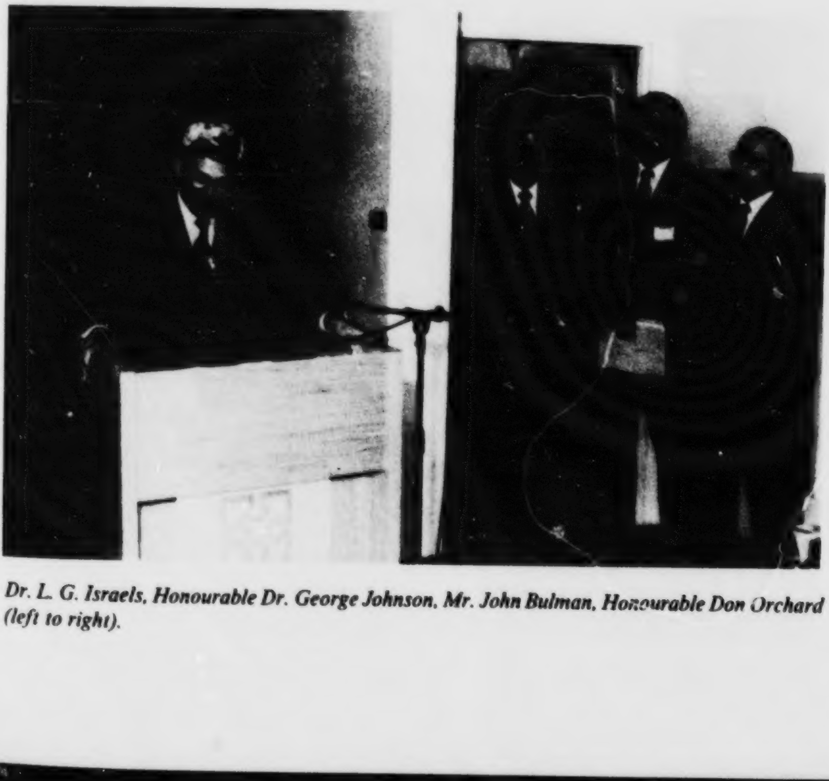
Dr. A. Zipursky (Hospital for Sick Children & University of Toronto) — "Dose Intensity and Survival in Children with Acute Leukemia".

Dr. E. Bow (University of Manitoba) — "Marrow transplantation in Refractory Malignant Disease".

Dr. H. Schipper (University of Manitoba) — "How to Do a Quality of Life Clinical Trial".

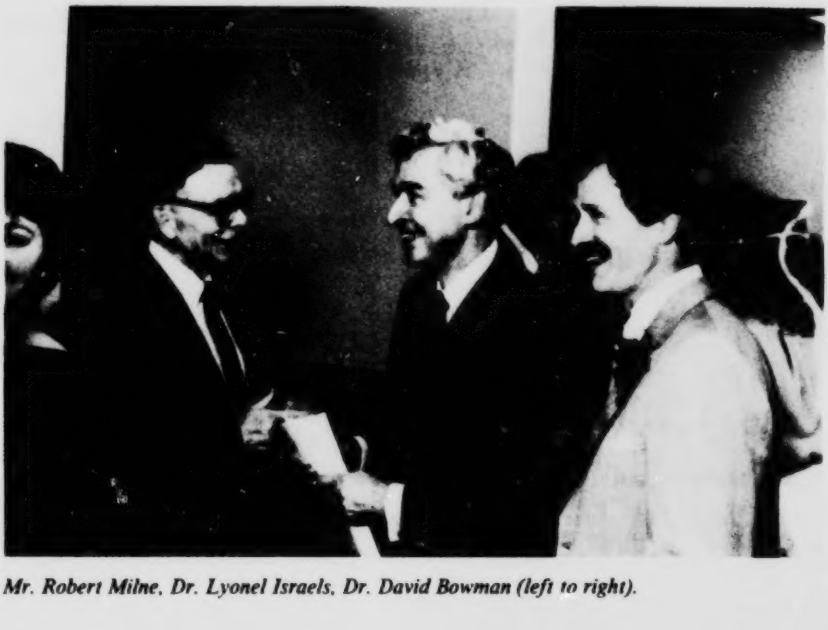
Following the scientific proceedings, some 200 guests participated in a dinner and Festschrift held at the Westin Hotel. The evenings' memorable events, chaired by Dr. Agnes Bishop included addresses by Dr. Arnold Naimark, President, University of Manitoba and the Honourable Don Orchard, Minister of Health and Social Services, who installed Dr. Israels as a Member of the Order of the Buffalo on behalf of all Manitobans.

Dr. Lyonel Israels is truly the Father of Oncology in Manitoba, and we salute his leadership in patient care, research and teaching as Section Head of Hematology-Oncology at the University of Manitoba 1960-1987.



Dr. L. G. Israels, Honourable Dr. George Johnson, Mr. John Bulman, Honourable Don Orchard (left to right).

Mr. Dennis McMullin, Dr. Arnold Naimark, Dr. David Bowman, Dr. Lyonel Israels (left to right).



Mr. Robert Milne, Dr. Lyonel Israels, Dr. David Bowman (left to right).

Honourable Don Orchard, Ms. Laurie Watts, Honourable Dr. George Johnson (foreground, left to right).

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PAEDIATRIC ONCOLOGY

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S. J. Israels, MD, FRCPC
N. L. Kobrinsky, BSc(Med), MD, FAAP, FRCPC
M. L. Schroeder, MD, FRCPC

ONCOLOGY NURSE

P. Pruden, RN

HOME CARE CO-ORDINATOR

K. McRae, RN

SOCIAL WORKER

S. Powell, MSW

CHILD LIFE THERAPIST

Dawn Kidder, CCLS

TEACHER

J. Wright, BA, BEd

DATA MANAGER

K. Hjalmarrson, HRT

OCCUPATIONAL THERAPIST

S. Hales, BMR-OT

RESIDENT

J. Gloor, S. Scott

SUPPORT STAFF

S. Snusher, J. Powell

PATIENT CARE

The Paediatric section is a major referral centre for children with oncological diseases in the Province of Manitoba and in Northwestern Ontario and has developed a comprehensive care programme for paediatric patients with cancer. Patients with haematological diseases such as chronic anemias and coagulation disorders also receive their outpatient care through the Foundation. Inpatient care is coordinated through the Children's Hospital while Ambulatory services are coordinated through the Cancer Foundation. The modern approach to treatment involves not only the medical aspect but also the psychosocial and developmental aspects of the patients and their families.

A multi-disciplinary treatment team is therefore involved in the care of the patients seen at the Foundation. The individuals involved include the Paediatric Haematologist/Oncologists, Oncology Nurse, Social Worker, Home Care Coordinator, Child Life Therapist, Teacher and Occupational Therapist. This team sees the patient whether the care setting is outpatient, inpatient or at home.

Pat Pruden, the Oncology Nurse from Children's Hospital, plays a major role, not only in the administration of chemotherapy, but also in the education of the patient and his or her family, friends and school with regard to illness, therapy and complications of therapy. She also provides inservice educational sessions for paramedical personnel who participate in the care of the child with cancer, and coordinates weekly meetings of the entire treatment team.

A major facet of her role is the coordination of the palliative care programme for the terminally ill child utilizing Ida Martinson's model for caring for terminally ill children at home. The majority of families have been able to keep their children at home up to, and often including, the time of their death, if it is their wish. In 1988, 5 children were cared for at home for periods ranging from two weeks to six months prior to their death. Due to the generous support of the Children's Chemotherapy Fund, two patient-controlled analgesia pumps were purchased, enabling those children who required pain management to remain at home. With this program in mind, Pat attended the First International Pediatric Pain Symposium in Seattle and the King's College Conference on Children, Death and Bereavement.

The psychosocial support services continue to be provided largely by one social worker, Susan Powell, from the Children's Hospital. The service fully recognizes that a life-threatening illness in a child has major implications for the entire family, not only while the child is on active treatment, but also when treatment is completed or the child has died. Every family has an opportunity to meet with the social worker, and if, necessary, counselling services are initiated for the patient and other family members. The social worker is an essential liaison with Children's Hospital in community resources to assist families with practical and emotional support. The teen group facilitated by Susan Powell meets several times over the year and has continued to be an invaluable support system for the adolescent patients. Susan attended the King's College Conference and a National Meeting on Children's Cancer Camps.

Susan Hales, an occupational therapist from Children's Hospital has been assigned to Paediatric Oncology. Her major patient referrals have been those with chemotherapy-related neurotoxicity, or with disease-related deficits. Developmental assessments, splints, special wheelchairs, and modification of home surroundings, are all activities for which Susan is responsible. She also provides a valuable liaison with community agencies for special needs patients. Susan attended a seminar in New York on Occupational Therapy for the Neurologically Impaired.

The child life therapist, Dawn Kidder, from the Children's Hospital is assigned halftime to the Cancer Clinic. The role of the child life therapist is to work with the patients and their families to reduce the stresses and anxieties they may encounter. She provides interventions designed to help children learn appropriate coping skills. Currently Dawn Kidder is offering a movement class "clownercise" for chronically ill children ages 4 to 8. The class provides opportunities for children to share feelings, learn about how their bodies function and how to learn and practice relaxation skills through play and movement. The child life therapist also maintains a welcome waiting room environment and coordinates special events such as birthdays. She also maintains a liaison with the Child life therapists on the wards of the Children's Hospital and with Jeffrey's Folks, the parents' self-help group. Dawn Kidder is a member of The Association for the Care of Children's Health. She provides training for volunteers and paramedical students and has presented at Nursing Grand Rounds, Subspecialty Rounds and the Hemophilia Week-end Seminar.

Children who are under care at the Cancer Foundation are strongly encouraged to carry out as normal a lifestyle as possible, including regular school attendance. Five years ago, a teaching position (funded by the Department of Education) was added to the Paediatric Oncology team. While in hospital, children are kept current in their school program, either by provision of one-on-one tutoring, or where it is appropriate, to involve the child in the classroom located in Children's Hospital. Ongoing liaison with the home school is maintained. Each year numbers increase as new cases are identified. The oncology nurse and the teacher, Joyce Wright, are able to visit schools anywhere in the province thanks to a grant provided by the Canadian Cancer Society, Manitoba Division. The team develops a supportive school and community climate, helping both the teachers and classmates understand and be more comfortable with the child with cancer. Follow up visits are made when there are changes in treatment which necessitate adaptive programming, when a child moves from one grade to the next, or from elementary to junior high. Joyce Wright provides assistance in helping the school and teachers deal with the terminally ill child. Some classes come to the clinic area where they observe first hand the treatment being received by their classmate. The visit is incorporated into the health curriculum as children complete assignments upon their return to school. An annual workshop ("Living with the Child with Cancer") has attracted principals, teachers, guidance counsellors and aids from various parts of the province. Presentations at conferences and networking with counterparts in other regions of Canada helps to keep information on cancer current. Research articles on the effect of treatment on learning are monitored and relayed to the concerned educators.

The Home Care Department of the Children's Hospital receives referrals from various sources, including physicians and nurses. The child and family are assessed, needs are identified and appropriate aid put into place after consultation with the Paediatric Oncology team. Home care becomes involved with children at varying critical times, such as diagnosis, during relapse or during palliative treatment. Services may include supplies, equipment, nursing visits and respite care. The Paediatric Home Care Program based at Children's Hospital is part of the Provincial Home Care Program administered through the Office of Continuing Care.

The oncology team has been instrumental in establishing three camps. The Children's Camp for patients and siblings at Arnes, Manitoba, is funded through the generosity of the Canadian Cancer Society and the Fehr and Janzen families. Last year 150 oncology and hemophiliac patients and siblings attended with 50 staff volunteers. In the spring there is a weekend camp for adolescents and young adults, held at Gull Harbour, which is also funded by the Cancer Society. Both camps combine fun and workshop activities. Jeffrey's Folks, the parents' support group, has a family weekend camp at Lakeside in the fall, funded by the Cancer Society. This is an ideal opportunity for the families to get together in a relaxed environment. Jeffrey's Folks have initiated a visitor's program in which a trained volunteer parent will make contact with all new families. This program has been successful in increasing awareness of the various support groups available, and significantly reducing the sense of isolation many families experience at the time of diagnosis.

The Section of Paediatric Oncology is affiliated with the Children's Cancer Study Group which consists of numerous institutions involved in paediatric cancer treatment throughout North America. As a member of this group, we participate in treatment protocols designed to provide children with cancer with up to date treatment. Over the past year, a number of developments have occurred in the treatment of children with malignant tumours. A number of studies designed to evaluate optimal therapy for children with acute lymphocytic leukemia (ALL) are now complete. These studies confirm that intensive consolidation and delayed intensification therapy improve long term survival in average and high risk patients. The clinical trials furthermore indicate that the main component that has improved survival is delayed intensification therapy (ie. complete reinduction after initial remission has been achieved). With the addition of the delayed intensification phase, the overall disease free survival of three years with ALL is approximately 75-80%. In acute non-lymphocytic leukemia (ANLL) on the other hand, results are not as good with the initial induction rate being approximately 75% and long term survival being approximately 45%. In an attempt to improve the induction rate, a new chemotherapy regimen has been developed in Winnipeg. The initial pharmacological studies which confirmed that the three drugs being used could be mixed in a single bag was also performed in Winnipeg. This regimen is now being piloted by several institutions in the Children's Cancer Study Group with hope of attaining better long term results in this type of leukemia as well.

Major improvements have also occurred in other diseases such as the soft tissue sarcomas, non-Hodgkin's lymphoma, neuroblastoma and brain tumours. It is only through collaborative studies that we can continue to progress and hopefully cure increasing numbers of patients.

The Paediatric Haematologist/Oncologists are also responsible for the diagnosis and treatment of children with disorders of blood coagulation. Approximately thirty children per month are seen at the clinic for an initial evaluation or subsequent treatment for these disorders. Further evaluation of the families is often carried out, as many of these disorders are hereditary. Appropriate pre-operative treatment to prevent excessive bleeding at the time of surgery has become an important service provided to this group of patients.

During the last year, studies of platelets and malignancy have continued. A significant contribution was work on the role of histamine as an intracellular messenger in platelets. A manuscript describing initial studies on platelets was published in Cancer Research, and a paper was presented at the American Society of Hematology, describing these further results. In addition to this work, studies of the growth of bone marrow cell subpopulations and the effects of superoxide dismutase continue, and results of studies in relation to a possible mechanism of action of intracellularly phosphorylated tyrosine residues in contributing to cell growth and malignancy were published. Also completed and published, was a review of the Manitoba B.Sc. Med Program, a program which each summer provides several students to the Manitoba Institute of Cell Biology. This review of the B.Sc. Med. Program showed it was remarkably effective in promoting subsequent research careers.

Full support is available from the Department of Paediatrics, University of Manitoba in essential subspecialties such as immunology, allergy, infectious disease, neurology, genetics, endocrinology, surgical subspecialties, metabolism, nutrition and child development.

The Section is grateful for the support and cooperation of Administration of the Foundation, the Children's Hospital and Winnipeg School Division No. 1, in allowing personnel to cross institutional, geographical and functional boundaries, since, without this support, true comprehensive care for the paediatric oncology patient would not be possible. The Section is also grateful to the Canadian Cancer Society for the assistance which it has given us in the development of many of our support programs.

TABLE 1
Outpatients Seen in the Paediatric Haematology/Oncology Clinic

Visits	New	Follow-up	Nursing Chemotherapy	Total
1986	223	2,057	1,847	**4,127**
1987	274	2,148	3,160	**5,582**
1988	266	2,367	3,003	**5,636**

EDUCATION

The Section is fully approved for sub-specialty training by the Royal College of Physicians and Surgeons of Canada, and as a Section of the Department of Paediatrics, University of Manitoba, the teaching and educational programs of the Foundation for medical personnel include:

(a) Training of career paediatric haematologist/oncologists in preparation for careers in clinical practice, teaching and research. All candidates must conform to university entrance requirements for post graduate medical trainees and must have completed their core general paediatric training.

(b) The exposure of other oncology trainees (internal medicine, radiotherapy, surgery) to the paediatric oncology patient.

(c) The provision for general paediatric residents of sufficient and appropriate exposure to modern haematology and oncology.

(d) The training of basic scientists in research encompassed within the discipline of paediatric haematology/oncology.

The Paediatric Section also participates in a formal elective program for students from the University of Manitoba School of Nursing.

The participation of the nurse, social worker, teachers, play coordinator and parents in the education of their colleagues, the patients and their families has been discussed previously.

RESEARCH

In 1988, funding awarded to the Section for research projects totalled $382,000.

1. Children's Cancer Study Group: Affiliated member since 1978. All new patients are registered with CCSG and approximately 85% of patients are on study protocols. A. Bishop, N. Kobrinsky, S. Israels, M. Schroeder.
2. Platelets, natural killer cells and malignancies. J. Gerrard
3. The balance of prostacyclin and thromboxane in cardiovascular disease. J. Gerrard
4. Bleeding during tonsillectomy/adenoidectomy risk assessment and treatment. J. Gerrard
5. The influence of diet on bleeding time and bleeding symptoms in individuals with bleeding disorders. J. Gerrard
6. Epidemiology of hypertension in pregnancy among the Inuit, and the possible influence of diet. J. Gerrard
7. Membrane microfilament interaction in human blood platelets. S. Israels
8. Neonatal platelet function. S. Israels

9. Prevention and Treatment of Diabetes Mellitus in BB Wistar Rats with 2'-Deoxycoformycin (DCF). N. Kobrinsky
10. The influence of diet cn bleeding time and bleeding symptoms in individuals with bleeding disorders. N. Kobrinsky
11. Blood drawn from tonsillectomy/adenoidectomy recent assessment and treatment. N. Kobrinsky
12. The psychosocial effects of paediatric cancer on healthy siblings and the family. N. Kobrinsky
13. HLA and disease. M. Schroeder
14. Role of platelet antibodies in the pathogenesis of intracranial hemorrhage in the neonate. I. Bonacossa, J. Yager, M. Schroeder
15. Flow cytometric test for platelet alloimmunization. S. Stewart, M. Schroeder

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SURGICAL ONCOLOGY

SECTION MEMBERS:

W. A. Beecroft, DDS, MD, FRCSC, FACS
B. J. Anderson, MD, FRCSC, FACS

NURSING STAFF:

J. Kostenuik, R. N., L. Scott, R.N.

SECTION OF SURGICAL ONCOLOGY

ORGANIZATION

The Section of Surgical Oncology provides consultative services and clinics five days a week at The Manitoba Cancer Treatment and Research Foundation. Active involvement in the Head and Neck Tumor Conference and Clinics continues. Biopsy and endoscopy services are provided in the Procedure Room at the Foundation.

Frequent multidisciplinary consultations with Radiation Oncology and Medical Oncology are carried out. Surgical procedures, both diagnostic and therapeutic are carried out at the Health Sciences Centre as part of the Surgical Oncology Service function of the Section of General Surgery.

In 1988 a Surgical Oncology/Radiation Oncology ward was established at the Health Sciences Centre. This dedicated ward will improve patient care as well as provide significant improvement in our training programs.

TEACHING

The resident and undergraduate house staff from the Surgical Oncology Service at the Health Sciences Centre participate in the Head and Neck Tumor Conference and Clinic as well as the other Surgical Oncology Clinics. Postgraduate training of General Surgery Residents as well as Otolaryngology Residents continues. Other residents rotate through the service from Oral Surgery, Radiation Oncology and Medical Oncology. Clinics provide experience in new patient evaluation, multi-disciplinary consultation, and patient follow-up in a wide variety of malignant diseases. There are multi-disciplinary ward rounds in the Surgical Oncology/Radiation Oncology wards as well as weekly teaching audit rounds.

CLINICAL INVESTIGATION

Active participation in the numerous NSABP Breast Cancer Trials and Colo-Rectal Trials is promoted. Continued interest in developing further Head and Neck Oncology protocols as well as other protocols for the management of malignant disease is promoted.

SECTION OF SURGICAL ONCOLOGY STATISTICS

Manitoba Cancer Treatment and Research Foundation

	New Patients	Follow-up Visits	Total Patient Visits
1983	217	784	1,001
1984	287	1,225	1,512
1985	417	1,660	2,077
1986	477	2,113	2,590
1987	580	2,561	3,141
1988	665	2,746	3,411

Diagnostic Outpatient Procedures

	Endoscopy	Biopsy	Total
1983			152
1984	11	182	193
1985	36	247	283
1986	58	270	328
1987	68	301	369
1988	63	371	434

HEAD AND NECK TUMOR CONFERENCE AND CLINIC

Dr. W. A. Beecroft and Dr. K. D. Jones — Joint Coordinators — 1988

The weekly Head and Neck Clinic, which was established in 1971, continued through 1988. Staff members from the Manitoba Cancer Treatment and Research Foundation and the Health Sciences Centre, with a special interest and expertise in head and neck oncology attend each Thursday morning. During a formal Conference, the relevant pathology and radiology is reviewed. This is followed by a discussion aimed at developing a consensus in a multi-disciplinary setting, for the optimum management of each patient. The follow-up clinic is held following this Conference at which time previously treated patients and patients undergoing treatment are reviewed.

The Clinic and Conference continued to be busy with 170 patients being presented at the formal Conference and a total of 1,783 patient visits being recorded in the follow-up clinic during 1988. We would like to thank the nursing and administrative staff for their help in organizing this weekly undertaking.

The formal Conference presentations continue to be chaired in rotation by representatives of the Surgical Oncology and Radiation Oncology sections. We would like to thank Drs. MacEwan and Alguacil for their invaluable help with the Radiology and Pathology portions of the Conference. Participation by the Section of Dentistry and Nursing is greatly appreciated.

GYNECOLOGICAL ONCOLOGY

SECTION HEAD:

Garry V. Krepart, M.D., B.Sc.(Med.), F.R.C.S.(C), F.A.C.O.G.

SECTION MEMBER:

Robert Lotocki, M.D., B.Sc., F.R.C.S.(C)

CLINICAL FELLOWS:

Dr. P. Ghatage, F.R.C.S.(C), Dr. M. Heywood, F.R.C.S.(C)

RESIDENTS:

Dr. Chan, Dr. Wong, Dr. Glowacki, Dr. Pokrant

NURSING STAFF:

I. Chrunyk, B. Lucko

NURSING AIDES:

I. DeSousa

SECTION OF GYNECOLOGIC ONCOLOGY

ORGANIZATION

The Section of Gynecologic Oncology is represented at the Manitoba Cancer Treatment and Research Foundation as well as at the St. Boniface Oncology Unit, at the Health Sciences Centre and St. Boniface General Hospital. Members belong to the Section of Gynecologic Oncology of the Department of Obstetrics, Gynecology and Reproductive Sciences of the Faculty of Medicine. Clinics are held four one-half days weekly at the Manitoba Cancer Treatment and Research Foundation and three one-half days at the St. Boniface Oncology Unit. Close liaison is maintained with the Radiotherapy and Medical Oncology Divisions as well as urologic and surgical oncologists at both institutions. Referred patients are seen at both Oncology units and appropriate consultations, if needed, with other divisions. Hospital admissions are at the Women's Hospital or at St. Boniface Hospital. An Oncology Unit as well as a high-dependency area and a dedicated in-patient chemotherapy nurse is available at the Women's Hospital with similar facilities at St. Boniface Hospital on the Gynecology Service.

TEACHING

Various levels of teaching are offered by the Gynecologic Oncology Service. A two-year postgraduate Fellowship Program was established in 1981. Currently the program has two Fellows, with a new Fellow for 1989-91. Dr. Ghatage entered a two year Fellowship in July, 1987, Dr. Heywood in July, 1988.

Residents in their third and fourth year rotate through the Section for three month rotations as part of their training in the Department of Obstetrics, Gynecology and Reproductive Sciences. Tumor Conferences are held weekly at the Women's Hospital and St. Boniface Hospital with much appreciated pathology backup by Dr. M. Paraskevas and by Dr. G. Vadas. Reviews of current subjects in Gynecologic Oncology or pertinent clinical cases are presented for all residents, medical students, interns and staff.

The Section is responsible for chemotherapy as well as surgery. Bowel as well as urinary complications, as they relate to gynecologic malignancy or its treatment complications, are handled at both teaching hospitals. Full support is available from all subspecialty areas, including T.P.N., Infectious Disease, Surgery, Urology and Physiotherapy. Full access to medical workers, chaplaincy service, pharmacy, occupational therapy and dietetics is available and a weekly nursing conference with all support staff represented is held. More then 1,200 in-patients were admitted in 1987 at both the Women's Hospital and St. Boniface Hospital units.

CLINICAL INVESTIGATION

The Section is active in the N.C.I.C. Ovarian Cancer Protocols, both at the level of the writing committee and patient treatment.

Other interests of the Section include:

a) Surgical staging and endometrial carcinoma.

b) Place of second look laparotomy in cancer of the ovary.

c) Chemotherapy treatment of ovarian sarcomas.

d) Frequency of cervical cytology.

e) Colposcopy in preinvasive cervical lesions and the use of laser in cervical, vaginal and vulvar preinvasive disease.

f) The role of staging laparotomy in early ovarian cancer.

g) The role of chemotherapy in ovarian carcinoma of low malignant potential.

h) Chemotherapy of Uterine Sarcoma.

Clinic Visits

	New Patients	Follow-up Visits	Total Patient Visits
1987	303	3,465	**3,828**
1988	408	3,391	**3,799**

Colposcopy Clinic

New	Return	Total
501	2,039	**2,540**

Hospital Admissions — 1988

	Health Sciences Centre	St. Boniface General Hospital	Total
Surgical	399	275	**674**
Non-surgical	464	92	**556**
Total	**863**	**367**	**1,230**

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NEURO-ONCOLOGY

CHEMOTHERAPY

Nathan L. Kobrinsky, M.D.

NEUROSURGERY

Derek Fewer, M.D.

NEURORADIOLOGY

William, Gordon, M.D.; Alice Patton, M.D.

RADIOTHERAPY

Keith Jones, M.D.; Kalyani Vijay, M.D.; Kamal Malaker, M.D.

NEUROLOGY

Fran Booth, M.D.; Shashi Sesha, M.D.; George Derbyshire, M.D.

INTERNAL MEDICINE

Norman Hechtenthal, M.D.

PHARMACY

Diana Dickof, B.Sc., B.Sc.Pharm.

NEURO-ONCOLOGY NURSE PRACTITIONER

Janice Lutz, R.N.

CHEMOTHERAPY NURSING

Nancy Johnson, R.N.; Jolene Cherland, R.N.; Susan Borrett, R.N.

RADIOTHERAPY NURSING

Ellen Nelson, R.N.

CLINICAL ASSISTANT

Linda Jonasson

STATISTICIAN

Mary Cheang, M. Math.

The Neuro-oncology clinic was established in an attempt to provide a comprehensive, multi-disciplinary program for patients with malignant brain tumors (Table 1). Prior to this time, a co-ordinated treatment program did not exist and therapy was oftentimes determined by the vagaries of patient referral, rather than by a co-ordinated team approach.

From its inception the clinic has been extremely successful. Virtually all patients with newly diagnosed and recurrent brain tumors are now seen in the Neuro-oncology clinic. Each patient is evaluated at the time of diagnosis and at regular intervals thereafter, at the preclinic conference.

The Neuro-oncology conference has grown in popularity over the year and now is widely attended. Participants from all related disciplines, including chemotherapy, neurosurgery, neuroradiology, neuropathology and radiotherapy participate.

In addition to providing uniform and state of the art care from the medical point of view, the clinic also provides important psychosocial support for patients as well. Input by psychiatry and social work have been important aspects of the program.

Clinical Research

Creation of a comprehensive clinic has also permitted the development of a clinical research program to improve the outlook for patients with malignant brain tumors. Since January, 1987, all newly diagnosed patients with malignant brain tumors have been treated with surgery, radiation and adjuvant chemotherapy. The adjuvant chemotherapy used has been a modification of the "8 drugs in 1 day" regimen, which was originally developed in Seattle for treatment of children with malignant brain tumors. Using this approach, the progression-free survival and overall survival of patients with malignant brain tumors, has been significantly improved, compared to results obtained using surgery and radiation therapy alone. Despite the intensity of the chemotherapy treatment, patients have found the program tolerable, and without question, quality of life has been significantly improved.

For patients with recurrent malignant brain tumors, the "8 in 1" schedule has been even more impressive. Of eight patients treated, complete radiological disappearance of the tumor has been observed in four, and a major response has been observed in two patients [Figures 1(a) and (b)].

Preliminary results of the "8 in 1" treatment have been presented at the Third Canadian Neuro-oncology Meeting in London, Ontario (June 9, 10, 1988) (see abstract).

Recent Developments

Nursing Clinic Rounds

The neuro-oncology clinic gives the nurse welcome opportunity to practice a full spectrum of skills, including direct patient care, teaching and counselling. Nursing rounds are held weekly and are attended by the pharmacist and nursing team. Our goal is to broaden this perspective to include representatioves from social work, home care and physiotherapy. Presently, the team focuses on intense follow-up of each neuro-oncology patient through the course of chemotherapy and radiotherapy, identifying problems encountered by patient and family with referral to appropriate support services. Our intent is to develop a program which provides continuity of care, while preserving quality of life.

Psychosocial Support

Two volunteers have recently expressed interest in joining the neuro-oncology team to provide psychosocial support for patients and families with brain tumors.

Neuro-Oncology Conference

Drs. Sutherland, Fewer, Gordon and Kobrinsky will be organizing the Fourth Canadian Neuro-oncology Meeting, to be held in Winnipeg in the spring of 1990. Individuals interested in helping organize the conference should contact one of these conference coordinators.

Clinical Care and Research

An NCI trial for the treatment of patients with oligodendroglioma has recently opened. The Manitoba Neuro-oncology unit will be enrolling patients on this trial. Over the past year a number of adjuvant chemotherapy drug combinations have been evaluated in the neuro-oncology clinic. These combinations have included cis-platinum, etoposide and high dose Ara-C ("Ape"), cis-platinum/etoposide (PE), ifosfamide/mesna/etoposide (IE), cyclophosphamide/etoposide (CE), and thiotepa/etoposide (TE). A prospective, randomized trial is proposed to begin in 1989 or early 1990. This trial will compare ifosfamide and etoposide administered over 5 days with cyclophosphamide and etoposide administered over 5 days and with cyclophosphamide and etoposide administered on a single day. This trial will establish the relative efficacy of ifosfamide compared with cyclophosphamide and will also establish in general terms whether single day or five day therapy is optimal for patients with malignant brain tumors. Both of these study questions will have potential applicability for other tumors types.

ABSTRACT

IMPROVED SURVIVAL IN ADULTS WITH MALIGNANT GLIOMAS TREATED WITH RADIATION THERAPY AND MODIFIED "8 DRUGS IN 1 DAY" CHEMOTHERAPY

Nathan Kobrinsky, Janice Lutz, Derek Fewer, William Halliday, William Gordon, Kamal Malaker, Keith Jones, Kalyani Vijay, Mary Cheang, Norman Hechtenthal, Linda Jonasson, Nancy Johnson, Diane Rumpel.
Neuro-oncology Clinic, Manitoba Cancer Treatment and Research Foundation, Winnipeg, Manitoba.

Seventeen adult patients with high-grade gliomas diagnosed in 1987 were treated with an intensive multi-agent chemotherapy (CTX) regimen following completion of standard radiation therapy (SRX). The chemotherapy regimen was based on a modification of the "8 in 1" regimen, developed in Seattle, for treatment of pediatric patients, and included vincristine, procarbazine, hydroxyurea, CCNU, methylprednisolone, carboplatin, decarbazine and cytosine arabinoside, administered with mannitol diuresis over six hours, every six weeks for a total of eight courses. The outcome of these patients was compared to historical controls treated in 1985 and 1986 with SRX alone (twenty-three patients), or with hyperfractionated radiation therapy (HRX) (twenty patients). Patients in the SRX and HRX groups had similar outcomes (progression-free survival 17.0 ± 2.6 vs 24.0 ± 3.4 weeks, $p = .73$; overall survival, 36.0 ± 3.2 vs 34.5 ± 3.3 weeks, $p = .91$), and were, therefore, combined for the purpose of subsequent analysis. The CTX and SRX/HRX groups were comparable for sex, extent of surgical resection, histologic grade and Karnofsky score. The groups differed in mean age (50 vs 60 years, $p = .01$) and radiation therapy dose (49.3 vs 54.6 Gy, $p = .0002$). Treatment with CTX prolonged progression-free survival (32.0 ± 2.8 vs 18.5 ± 2.4 weeks, $p = .008$), and overall survival (43.0 ± 2.7 vs 35.0 ± 2.4 weeks, $p < .04$), compared with SRX or HRX alone. Treatment with CTX also prolonged survival in eight patients with recurrent tumors, compared with thirty-four patients who did not receive salvage CTX (30.0+ vs 10.0 ± 2.1 weeks, $p = .0005$). CTX was administered on an outpatient basis in 24/82 (34%) courses. Progressive hematologic toxicity ($p < .05$), requiring dose reduction ($p = .001$) was noted with subsequent courses of therapy. Red blood cell transfusions following 3/80 (3.8%), and platelet transfusions following 9/80 (11.2%) courses of therapy, were required. Infections and deaths related to therapy were not observed. Based on the encouraging findings of this pilot study, a prospective randomized trial should be considered.

TABLE I
Malignant Brain Tumors, Manitoba Cancer Treatment and Research Foundation

	1985	**1986**	**1987**	**1988**	**1985-88**
Pediatric	4	2	6	5	17
PNET/Medulloblastoma	1	0	1	2	4
Ependymoma	2	0	2	0	4
Brain Stem Glioma	2	3	2	2	9
Oligodendroglioma	1	1	2	0	4
Malignant Meningioma	1	1	0	1	3
Astrocytoma and Other Malignant Gliomas	28	31	29	36	124
Total	**39**	**38**	**42**	**46**	**165**

Average 41 cases/year.

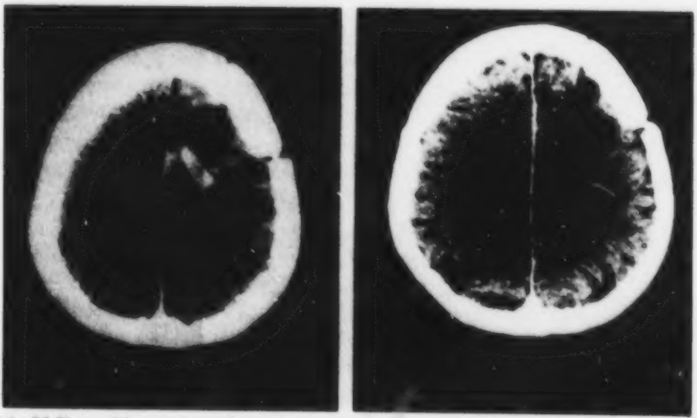

Fig. 1(a). *55 Year old woman with recurrent glioblastoma multiforme demonstrating complete resolution of her tumor following 8 courses of "8 in 1" chemotherapy.*

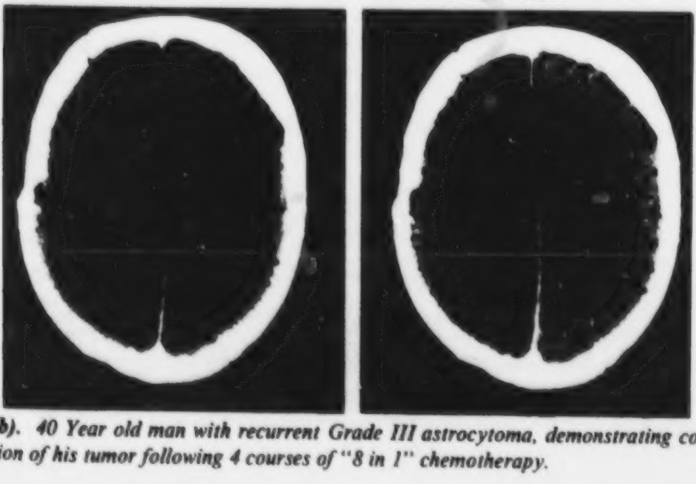

Fig. 1(b). *40 Year old man with recurrent Grade III astrocytoma, demonstrating complete resolution of his tumor following 4 courses of "8 in 1" chemotherapy.*

ONCOLOGY NURSING/TECHNOLOGY

Director of Nursing: B. Glenday, R.N.
Assistant Director of Nursing and Clinical Investigation Liaison Nurse: J. Lutz, R.N.
Department Secretary: S. Burgess

MEDICAL ONCOLOGY:

N. Johnson, R.N., Senior Nurse
S. Borrett, R.N., S. Bracken, R.N., L. Friesen, R.N.
D. Rumpel, R.N., S. Switzer, R.N.

Clinical Assistants:
I. DeSousa, G. Harney/C. Jones, L. Jonasson, U. Merck

Clinical Investigation:
K. McDonald, R.N., Senior; V. Powell, R.N., S. Borrett, R.N.

Gynecological Oncology:
I. Chrunyk, R.N.

Pediatric Oncology:
P. Pruden, R.N.

Receptionist:
C. Jones/M. Powder

RADIATION ONCOLOGY:

M. Chambers, R.N., Senior Nurse
B. Dodds, R.N., S. Kelly, L.P.N., J. Kirbyson, R.N., R.T.T., E. Nelson, R.N.

Surgical Oncology:
J. Kostenuik, R.N., Linda Scott, R.N.

Clinical Assistant:
I. Turnbull

Unit Assistant:
M. Corden

Receptionist:
M. Cabral

Radiotherapy Technologist Training Program Coordinator:
E. Kirk, R.N., A.C.(T)

Radiotherapy Technologists:
Supervisor — J. Howes, R.T.T.
Senior Technologists — K. Fox, R.T.T./J. Halfdanson, R.T.T., S. Ryder, R.T.T./
G. Kowaski, R.T.T., Tracy Maciboric, R.T.T.
Technologists — D. Bettig, R.T.T., T. DePape, R.T.T., H. Doherty, R.T.T.,
T. Engel, R.T.T., J. Friess, R.T.T., J. Grestoni, R.T.T., D. Hughesman, R.T.T.,
C. Marlowe, R.T. (R&T), D. Swanson, R.T.T., P. Thomson, R.T.T., K. Wedlake, R.T.T.

Student Radiotherapy Technologists:
K. Balak, C. Hall, S. Johnson, B. Lucyshyn, C. Sveinson (First Year)

ST. BONIFACE NURSING AND TECHNOLOGY STAFF:

G. Ogilvie, R.N., R.T.T., Senior Nurse, B. Lucko, R.N.
S. Hatton, R.N., R.T.T., Senior Technologist, R. Olson, R.N., R.T.T.,
S. Sharpe, R.T. (R&T).

ONCOLOGY NURSING TECHNOLOGY

The nursing and technology staff continue to strive to provide the optimum of care for our patients. To meet this commitment and to keep abreast of current trends and issues of the 80's the staff attend as many educational sessions as time and financial support permit. Cancer Foundation Nursing staff were represented at the American Urological Conference, Boston, Massachusetts; The 1st CANO Conference, Vancouver, B.C.; Psychosocial Conference, Montreal, Quebec; 5th International Conference, London, England; NSABP meeting, Washington, D.C.; and the 3rd Neuro-Oncology Meeting, London, Ontario. Technologists attended the Wescan Conference, Regina, Saskatchewan; The ASTRO Meeting, New Orleans, Louisiana and the CAMRT meeting in Vancouver, B.C. The financial support to attend the majority of those meetings was provided by the Nursing/Technology Education Fund. This money has been successfully raised solely by fund raising endeavors of the staff. Staff also attend inservice and continuing education sessions held on a regular basis throughout the year.

We continue to provide a three day seminar "Cancer Care — A Multi-Disciplinary Approach" for health professionals working with cancer patients. The sessions are well attended and are followed by a three week practicum. This portion of the program is designed for those nurses who are entering the field of Oncology Nursing and who will be working in settings where antineoplastic agents will be administered.

Lectures on cancer, care and treatment of the patient with cancer requested by other facilities and allied health care professionals continue to be provided by the staff.

The Brain Tumor Clinic, a multi-disciplinary team, coordinated by nursing staff continues to provide improved quality of care for the patient. The combined approach brings together nurses, social workers, neurosurgeons, pathologists, radiologists, radiation and medical oncologists, from both adult and pediatric discipline to a weekly conference, followed by the clinic. The nurse coordinator is instrumental in organizing the content of each conference, describing histories and leading the discussion which often becomes an informal learning experience. A clinical evaluation form was designed by J. Lutz, with a research study in mind.

Nursing interventions, utilizing effective antiemetic therapy have minimized the side effects and this reduced the number of hospital admissions, which contributes to decreased hospital costs. Other toxicities, not previously well documented have also been recognized.

Rounds are held weekly by the nursing staff to discuss problems which results in increased coordination of care. Patients are now closely monitored and families happier.

The number of patients treated with complex treatment regimes is increasing yearly. With careful planning and coordination of care the staff is able to keep patients comfortable at home. This is possible due to our dedicated, caring and knowledgeable staff.

Two Conjoint Clinics (Breast and Gynecology) have been introduced this year and the nurses are adapting well to the new format. Other conjoint clinics will be implemented.

Pediatric nursing, coordinated by Pat Pruden (addressed in the Pediatric Section) is a member of a multi-disciplinary team.

The nurses working in all clinics provide increasing patient support due to hospital early discharge programmes.

The clinical nurse specialist provides valuable assistance to the Medical Oncologists in clinical evaluation, furnishing the necessary liaison between patient care in clinic and investigation evaluation and management. She also supervises the nurse(s) involved in specific studies.

The radiotherapy treatment floor has experienced a number of staff changes again this past year. A receptionist position was finally approved which allows the technologists to work with fewer interruptions. Two shifts are still required on our high energy machine to cope with the patient load. Renovations were finally underway in the latter part of the year to accommodate the installation early in 1989 of a new unit. This has been accomplished with a minimum of inconvenience for both the technologists and the patients.

Competent and empathetic care is given by the technologists to the patients undergoing radiotherapy treatment. They also find time for those little extras that add to the patients quality of life even with an increased workload and the increasing complexity of today's treatments.

A refresher program is still offered to those interested in returning to the work force. We had one participant this year.

The Department of Nursing/Technology strives for excellence in all of their endeavors.

RADIATION THERAPY TECHNOLOGIST TRAINING PROGRAM

E. Kirk, R.N., A.C.(T), Radiotherapy Technologist Training Program Coordinator

Last year it was reported that we would be making major changes in the delivery of our training program in 1988. I am pleased to report that a number of these changes have been implemented and we anticipate that they will result in better use of time and resource as well as improved academic and clinical performance of our students.

In 1988, we accepted five students into the revised program which began on May 16. At the time of this report we have completed Terms I and II (Academics) and Clinical I, and so far all participants, both students and staff, have agreed that the changes have been positive. In addition, we have had two students from the Saskatoon Cancer Clinic join us for the academic terms. We welcomed Joe Andreas and Rob Thibault, and found that they brought with them new ideas and concepts which enhanced our programs, as students from different Clinical sites shared and challenged one another!

Four graduates of our program wrote and passed the National C.A.M.R.T. examinations in 1988. Our congratulations to Conny Speiss, Debbie Bettig, Leanne Radcliffe, and Deborah Willits. Special congratulations to Debbie Bettig who won the General Proficiency Award and Leanne Radcliffe who won the Essay Award, at the Annual M.A.M.R.T. Commencement Exercises in September.

It was with regret that we accepted the resignation of Mrs. Nancy Saunders as Deputy Program Coordinator, but wish her the best as she and her husband continue with their careers in Victoria.

HAEMATOLOGY LABORATORY

CHIEF TECHNOLOGIST

Elsa Friesen, A.R.T. (to October 31, 1988)

MEDICAL TECHNOLOGISTS

Marlene Crielaard, R.T.; Dianne Gamble, R.T.; Kim Gorski, R.T.; Jeannine Olivier, R.T.; Susan Tighe, R.T.; Leona St. Onge, R.T.

The Haematology laboratory is responsible for all the routine haematological investigations including bone marrow differentials for the out-patient population attending the radiotherapy and chemotherapy clinics within the Foundation. As a large percentage of these patients have abnormal blood profiles, visual differentiation of cell types and confirmation of values obtained by electronic counting is necessary. The presence of the laboratory in the clinic area enables a preliminary report to be available to the physician within five minutes of obtaining a blood sample making it possible for chemotherapy and radiotherapy to proceed on these patients without delay. The number of patients visiting the laboratory in 1988 was 20,182 as compared with 18,592 patient visits in 1987.

ONCOLOGY SOCIAL WORK

DIRECTOR — Betty S. H. Wong., M.S.W., R.S.W.

SOCIAL WORK STAFF

Leonard A. Perry, B.S.W.

SUPPORT STAFF

Anneliese Friedle, Secretary

Annual Report — 1988

Organization

Established in 1974 by the Health Sciences Centre and the Manitoba Cancer Treatment and Research Foundation, Oncology Social Work has continued to function as a joint program between the two institutions. The first director was hired by the Health Sciences Centre to coordinate the oncology social work program at the Manitoba Cancer Treatment and Research Foundation. This arrangement still continues to date and accordingly the director has a dual reporting responsibility.

Over the years social work consults continue to increase proportionately to the overall increase in cancer patient population. However, social work staff remains the same since 1981. In order to meet this heavy demand for services, oncology social work has to carefully examine it's priorities and provide services in such a way that quality of care is not being jeopardized. To be continuously faced with this challenge has not been easy. Many of the practical functions have to be streamlined and delegated to support staff allowing social work staff more time to deal with the counselling and psychosocial issues. Consequently the department has been able to meet the service commitments to the cancer patients and assistance to the community who seek our consultation.

Patient Care

Counselling Services are provided to cancer patients and their families who have difficulties coping with their disease at different stages of development. Some of them require brief but intensive counselling at the initial stage of diagnosis to cope with the initial shock; others require counselling to help sustain their families' emotional equilibrium during the period of remission; others require counselling in anticipation of their impending deaths and subsequent bereavement counselling for their families.

Referral Services: As long term treatments frequently interrupt productive employment, many patients do not have sufficient resources to support themselves and their families. Resource counselling is provided to those who experience financial difficulties during their illness. After proper assessment, referrals are made to the appropriate financial agencies.

Referrals are frequently made to the Homecare department to facilitate early discharges: This service leads to better utilization of beds and to enable patients to remain longer in the community. Some of the requests for practical services such as transportation between their homes and the clinic and temporary accommodation for out-of-town patients while on treatment, were referred to the Canadian Cancer Society Office located at the Foundation.

Discharge and Transfer to Other Institutions: Discharge planning for inpatients continue to demand a great deal of time. Many patients and their families find it difficult to accept their inability to function independently in the community and therefore would need alternative care. Palliative Care at the Princess Elizabeth Hospital is often one of the alternatives that they have great difficulty accepting. Both patients and families often need a great deal of supportive counselling in order to resolve their ambivalence regarding this placement. Actual transfers to the P. E. H. and other Health Care Institutions are handled by the social work assistant at the Health Sciences Centre.

Coordination: A multidisciplinary team is frequently involved in the care of inpatients at the Health Sciences Centre. Patients and their families often find it confusing and frustrating having to deal with so many people. To lessen these frustrations social work staff often become the facilitator communicating with disciplines involved in the care of patients.

Education

Social Work: Clinical Supervision — For years, the director has been on the clinical supervisory group for the University of Manitoba School of Social Work. It was decided this year that a few of us would take a break from this responsibility. The director was one of the supervisors who was on sabbatical during this last academic year.

Other Disciplines: Oncology Social Work continues to be involved with the education of students from other disciplines. These educational activities include inservice and informal classes as well as having students spend time in our department.

Other Activities and Developments

Oncology Social Work Rounds: Due to difficult time schedules and perhaps lack of interest, the weekly rounds with chemo nursing were sporadic during the year under review. However, weekly rounds with radiotherapy nursing and surgical oncology nursing have picked up momentum. The original purposes for these rounds: to provide better patient care through early problem identification, to facilitate interdisciplinary understanding and mutual s port and to provide an educational opportunity for student learning still hold true.

Brain Tumour Clinic: Due to staff changes and heavy case loads, social work has not been involved in this multidisciplinary team meeting as previously the case. However, we agree that there is great need for our participation in dealing with the psychosocial needs of these patients and their families. For the time being oncology social work shall continue to provid services to this group of patients on a referral basis.

Psychosocial Rounds: Oncology Social Work has been actively participating in these rounds held on H4, D6, H.S.C., chaired by Dr. Harvey Chochinov, psychiatric consultant for Medical Oncology. All those involved in these meetings agree that they are beneficial and necessary for communication and mutual support.

Membership in Professional Associations and Other Committees: The Director is a member of: The Canadian and Manitoba Association of Social Workers — The Canadian and Manitoba Association of Social Work Administrators in Health Facilities and — The Canadian Association of Psychosocial Oncology and The Manitoba Institute of Registered Social Workers. As a member of the M.A.S.W. Education Committee, her major contribution has been in the involvement of the Career Symposium, a yearly event sponsored by the School Counsellors Association and held at the Convention Centre in early February.

As a member of the former Palliative Care Committee of Health Sciences Centre, chaired by Dr. Leo Cruickshank, the director was invited to be on the Palliative Care Steering Committee when it was formed in early 1988, chaired by Mrs. Patricia Rae, Director of Medical Administration and subsequently chaired by Mrs. Donna Land, Senior Project Officer, Planning Department, H.S.C. Up to the end of the year under review, there was no definite response from M.H.S.C. regarding funding for the Palliative Care Program.

Both social work staff are members of the Oncology Social Work Interest Group.

Kids Can Cope Program

This new program was developed by Social Work and Nursing Staff of M.C.T.R.F. and St. Boniface Hospital for children 5-18 years who have a relative with cancer.

The program provides information about cancer and its treatment. It also provides a supportive environment whereby children can express their fears and anxiety with others in similar circumstances.

The planning group has decided to make this an ongoing program to run twice a year.

Community Liaison and Acknowledgement

Oncology Social Work continues to be involved in it's unofficial responsibility in Public relations. We have often been called upon to provide information and consultation to our colleagues in the community. Many non-patient related inquiries are often referred to this department for exploration and appropriate responses.

Oncology Social Work wishes to extend its sincere appreciation to the following — For their ongoing cooperation and assistance in our joint effort to provide quality care to our patient population:

— Canadian Cancer Society, Manitoba Division
— Volunteer Services, M.C.F.
— Our Social Work Colleagues at H.S.C.
— The Multidisciplinary team members at both institutions
— and our colleagues in the Social Work community.

Without their support, mutual understanding and collaboration, we would not be able to provide the excellent care to our patients as we have strived to do so.

Social Work Activities

	New Patients	Total Cases Opened	Total No. of Visits
1985	232		
1986	289		
1987	240		
1988	287	482	9,464

ONCOLOGY UNIT
St. Boniface General Hospital

Oncology Services Director:
H. Schipper, B.A.Sc., MD, FRCP(C)

Head Nurse — A. Meekison, R.N.

RADIATION ONCOLOGY

Radiotherapist — E. Baral, MD, E. Hadzic, S. Larsson, K. Jones
Radiation Technologists — S. Hutton, R.N., R.T.T., — Senior Technologist,
S. Sharpe, R.T.T., R. Olson, R.N., R.T.T.
Clinic Nurses — B. Lucko, R.N., G. Ogilvie, R.N.

MEDICAL ONCOLOGY

Physicians — E. Baral, M.D.
E. Bow, M.D., M.Sc., D.Bact., F.R.C.P.(C).
J. Foerster, B.Sc. (Med.), M.D., F.R.C.P.(C).
H. Schipper, B.A.Sc., M.D., F.R.C.P.(C).
A. M. Shojania, M.D., F.R.C.P.(C).
T. B. Shore, M.D., F.R.C.P.(C).
B. H. Weinerman, M.D., F.R.C.P.(C).
Nursing Staff — E. Bebchuk, R.N., Nurse Practitioner,
B. Scott, R.N. — Assistant Head Nurse, D. Self, R.N., I. Lemoine, R.N.,
A. Acheson, R.N.
Secretarial Staff — C. Prud'homme, B. Scott/R. Savoie,
K. Decosse/D. Mercredi, B. Coss

Support Staff — C. Berthelette, Senior Ward Clerk,
R. Provitina, Senior Ward Clerk, B. Marshall, Senior Ward Clerk, H. Lucy, NA II,
E. Deneweth, NA I.

Protocols — L. A. Love, Protocol Data Manager

SOCIAL WORK

J. Taylor-Brown, M.S.W.

ONCOLOGY UNIT — ST. BONIFACE GENERAL HOSPITAL

1988 marked something of a transitional year at the Cancer Foundation's St. Boniface General Hospital Unit. All aspects of the program are working at or close to full capacity. We continue to serve as the cancer treatment resource for the St. Boniface Hospital catchment area, and in addition, have over the years developed natural patterns of referral from Northwestern Ontario, and areas of Southeastern and South Central Manitoba. While there has been some increase in the number of patients seen in the Unit, the major ongoing development is a constant increase in the complexity of outpatient treatments administered, and the concomitant requirement for increasing levels of dedicated nursing, and psycho-social assistance.

Possibly the most important development of 1988 was the conclusion of the Integrated Oncology Program Agreement between the Manitoba Cancer Foundation and St. Boniface Hospital. This Agreement, which had been under discussion for approximately 2 years, forms the basis of a gradual, fundamental reorganization of cancer treatment within the institution. In particular, the focus will be on coordinated, multi-disciplinary management. Both inpatient and outpatient facilities will be developed and organized to optimize the input of medical professionals of numerous disciplines to the management of particular patients and disease sites. Administratively, the program is headed by a Director, and overseen by a Joint Advisory Committee composed of 3 representatives each of St. Boniface Hospital and the Cancer Foundation. While the program is intimately associated with the Department of Medicine, it seeks to involve physicians, surgeons and radiotherapists as a priori partners in the research and treatment process.

The program has a number of important components including Site Specific Working Groups, Integrated Multi-disciplinary Clinics, and rationalization of cancer treatment between the St. Boniface Unit, and the Health Sciences Centre Unit. In the first instance, multi-disciplinary expert working groups are being established with mandate to outline specific treatment approaches for individual diseases, and to provide direction and context for the clinical and laboratory research undertaken within those site areas. Where diseases are relatively uncommon, centers of excellence will be established where most patients will be treated. Second, the outpatient clinic will be reorganized so that chemotherapists and radiotherapists will work in a more integrated fashion. Where appropriate, Site Specific Clinics will be developed so that additional resources such as surgery, pathology, and radiology can be brought together in order that diagnosis and treatment can be coordinated from the outset. Sites targeted for this particular approach include G.I. tumors, and breast cancer.

In parallel with these developments, the hospital and the Cancer Foundation have committed to the establishment of an inpatient oncology unit within the next year. Detailed functional planning for this program, as well as the outpatient reorganization, is underway. The organization for this ward is under negotiation, but the goal is to provide a multi-disciplinary service, teaching and research environment for those cancers where multi-disciplinary input is most appropriate. In addition, the ward will provide the venue for the chemotherapy program and a expanded radiotherapy presence.

Since the expansion of the "O" Block was completed in 1984, the long-term goal of the program has been to expand and upgrade the radiotherapy service. The medical oncology profile has been strong. The provincial gynecologic/oncology service is shared between St. Boniface Hospital and the Cancer Foundation's Health Sciences Centre facility. In keeping with these long-term plans, functional planning for the installation of a dual energy linear accelerator at St. Boniface Hospital is in process. With its concomitant support services, the facility would have at its disposal, on site, the resources to meet any conventional radiotherapy need. This equipment could be operational in 1991. Concurrently, two full-time radiotherapists would be based at St. Boniface Hospital enabling the profile of radiotherapy to be raised, and an inhouse multi-disciplinary resource to be utilized.

The research and development activities at the St. Boniface Unit are part of an overall Cancer Foundation Program. They reflect the ongoing interests of senior medical staff based at St. Boniface. Some areas are highlighted:

1. Acute leukemia and the management of infections in the immunocompromised host. Our activity in this area have culminated in the evolution of standardized protocols for the management of acute leukemia patients, with close links to the marrow transplantation program of British Columbia. This provides both a treatment path for patients, and the basis of a data base for the evaluation of our results. The experience gained is critical to the development of marrow transplantation program to be located at the Health Sciences Centre D-6 Facility.
2. Many patients with acquired immune deficiency syndrome seek their treatment at St. Boniface Hospital. By virtue of a dual appointment in hematology/oncology and infectious diseases, Dr. Eric Bow has developed a substantial program in the area which serves the majority of Manitoba's small number of AIDS patients. The workload implications for physicians, nurses, and social workers have been considerable and the program and the hospital continue to make efforts to meet this need..
3. The clinical trials, and investigational drugs programs are actively carried on here. Large numbers of patients are entered into both National Surgical Adjuvant Breast Program, and National Cancer Institute (Canada) Phase III Programs, as well as smaller numbers into investigational drug programs involving both outpatient and inpatient clinical facilities. Department members play an active role in the conduct of these trials by virtue of memberships within the investigational groups, and service on protocol design, monitoring, and evaluation committees.
4. Quality of life studies is an area of research developed largely in Manitoba in which there has been considerable activity. Members of the department have been active in the development and implementation of quality of life methodologies as well as the conduct of specific trials. In particular, clinical trials are underway examining the quality of life implications of indwelling venous access systems, and the Outreach Program, among others.
5. Our chemotherapy nurses and nurse clinician, play an important research and development role in addition to performing their service functions. In particular, they have been active in the development of nursing standards and patient support systems. In addition, a number of significant nursing research studies continue to be conducted within the Unit.
6. Social Work. The professional staff allotment to social work within the Oncology Program is small, but the contribution is considerable. In particular, patients with immune deficiency syndrome require considerable support and assistance. Recently, also, the social work program has begun an expansion in order to serve the needs of radiotherapy, gynecologic oncology and marrow transplant patients. Research studies conducted by this group include investigations into support mechanisms for the children of patients with malignant disease.

The Oncology Program continues to grow. The next 2 to 3 years will offer a gradual transition from a satellite unit which was discipline oriented, to a self-sufficient facility whose orientation will be, *ab initio*, multi-disciplinary in all aspects: inpatient and outpatient; clinical treatment and research, and teaching.

Nursing

In accordance with the Aims and Missions of St. Boniface General Hospital and in collaboration with our multidisciplinary team (Social Work, Home Care, Pastoral Care, Palliative Care, Pharmacy, Dietetics), we strive to attain excellence in patient care. This year our team has further expanded to include Tracy Hildebrandt, Clinical Nurse Specialist, Medicine who is now further developing her role in the care of H.I.V. infected individuals in the outpatient Oncology setting. Her primary responsibilities for this patient population are to facilitate quality care for the patient/significant other, to coordinate ongoing educational programs and to liase with community resources.

June marked the publishing of the booklet, "Bone Marrow Transplantation — Information for Patients and Families" which was sponsored by the Canadian Cancer Society — Manitoba Division. Our nursing representative on the multidisciplinary committee which developed the booklet was Alma Acheson. Alma acts as primary nurse to Dr. T. Shore who is very active in the field of bone marrow transplantation.

"Kids Can Cope", a program of support sessions for children of cancer patients ran its first session in September. The six week pilot project, which was approximately eighteen months in the planning process, was a joint effort between M.C.T.R.F., S.B.G.H. Oncology and Social Work. The evaluations were excellent and sessions will be offered twice a year.

Monthly Nursing Grand Rounds, initiated in 1987, were well received and continue this year. The hour long inservice sessions address issues in the management of cancer patients. In addition to our multi-disciplinary team, an invitation has been extended to those areas in-hospital with whom we closely lease.

Our Out-patient Oncology Clinic Information Day continues to be provided as an ongoing basis to health care professionals within the hospital and the community. The day long inservice sessions includes the many disciplines which comprise our unit, provides an overview of cancer care and identifies internal and external support systems available for cancer patients/families.

Nursing continues this year its many collaborative activities:

i. Masters Program students (thesis projects)
ii. Schools of Nursing (B.N. R.N.)
iii. Public Relations Department (information tours)
iv. In-hospital consultative resource
v. Community consultative resource

We continue to place a strong emphasis on continuing education for staff members. In addition to regularly scheduled rounds (Oncology/Pathology Rounds, Psychosocial Rounds, Nursing Grand Rounds, "Dr. Bow/Shore" Rounds), staff members have attended several day long local educational sessions, one national psychosocial Oncology conference and one international cancer nursing conference.

In addition we are also active in providing continuing education sessions to the hospital and the community.

i. S.B.G.H. Monthly Support Group Meetings of Cancer Patients/Families — guest speakers

ii. Nursing Excellence Day — presentations

iii. Nursing Research Development Day — Collaborative presentation

iv. Second Annual Patient Education Exposition — display of resource material available to cancer patients/families

Of major importance this year was the implementation of Stage I of the Nursing Documentation Project. The project package consists of seven forms which have been developed to address the requirements for nursing documentation in the health record. The project has been divided into three stages to facilitate implementation. Stage II and Stage III are targeted for next year and will be our primary focus for 1989/90.

STATISTICS

TABLE I — Medical Oncology Statistics, St. Boniface Hospital

	New Patients	Follow-up Visits	Total Physician Visits	No. of Patient Treatments	Procedures
1981	224	2,242	2,466	2,326	N.R.
1982	306	2,580	2,886	2,152	N.R.
1983	377	4,257	4,694	3,753	3,399
1984	395	4,141	4,536	2,699	4,984
1985	492	4,656	5,148	2,475	9,483
1986	336	4,632	4,968	1,783	8,973
1987	353	4,673	4,939	1,797	9,303
1988	398	4,840	5,238	2,120	11,560

TABLE II — Protocol Statistics, St. Boniface Hospital — 1987

	On Study From End of		New Patients Entering During		Off Study During		Patients on Active Follow-up End of	
GROUP	1987	1988	1987	1988	1987	1988	1987	1988
NCIC	83	72	8	8	19	9	72	71
NSABP	119	122	10	14	7	6	122	130
RTOG	0	0	0	0	0	0	0	0
LOCAL & OTHERS	39	46	26	1	19	18	46	29
TOTAL	241	240	44	23	45	33	240	230

OUTREACH

Director — Dr. H. Schipper, B.A.Sc., M.D., F.R.C.P.(C)

Coordinator — Anne Nemecek, R.N., P.H.N.

Pharmacist — Diana Dickof, B.Sc., B.Pharm.

Data Manager — Cheryl Karaz, HRT.

Computer System Analyst — Bill Burgess

Secretarial Staff — Kathy DeCosse, Darlene Mecredi (Temporary),
Bonnie Coss (Cesmystruk) Newsletter Editor

The Outreach Program, the unique decentralized chemotherapy program of the Manitoba Cancer Treatment and Research Foundation provides cancer chemotherapy and symptom management to rural Manitoba cancer patients.

Chemotherapy is delivered at the Outreach Center by a team of trained physicians, nurses and pharmacists working under the direction of the urban oncologist. The oncologist outlines the treatment plan and the Outreach Center team implements the plan with the patient in his/her community.

Objectives of Outreach

The primary objective of the Outreach Program is to facilitate the delivery of cancer care throughout the Province without compromising the quality of care. The major component of this program is the parallel development of nursing, medicine, pharmacy and health records personnel. Continuing education for these professionals is provided according to their needs.

This year's achievements

The strategic plan of the Outreach Program was altered somewhat in 1988 when no formal expansion was approved. However, to plan ahead for the time when new centers could be added, a committee was struck to assemble a manual which would assist new centers in planning and implementing the Outreach Program within their facilities. The "New Center Manual" will be printed in early 1989.

The Outreach team worked diligently to revise the system for Outreach accrual, and to develop policies and procedures for the administrative, health records and data compounds of the program. The Pharmacy Reference Manual was completed in April 1988, and distributed to all centers.

The comprehensive data available through the statistical reporting system devised in 1987 has enabled us to monitor the activity of each Outreach center more closely. We saw an increase in the numbers of patients accrued to the program (Table I); as well as an increase in the number and complexity of treatment (see Table II).

Table I

No. of new patients entered on Outreach for chemotherapy	103
No. of patients entered on clinical trials through Outreach	15
No. of patients entered on Outreach for follow up	39
New patients	159

Table II

No. of chemotherapy treatments given in all Outreach Centers

1987 — 1,929
1988 — 2,065

The role of continuing education in Outreach is an important focus. In 1988 three new Outreach nurses were trained to deliver chemotherapy; and two Outreach physicians received additional training. Since 1987, six Outreach physicians have been successful in receiving the Stephen Fonyo Fellowship from the Canadian Cancer Society to offset the costs of their orientation periods. We held a two day symposium in April celebrating our first decade. Over seventy oncology-related health professionals attended the continuing education sessions. We are continuing our newsletter publication every three months.

Outreach has sparked interest in other provinces. Representatives from the London Regional Cancer Center, and the Alberta Cancer Board visited with the Outreach team in 1988 to learn about our program. Nurses from Brandon were invited to present in a poster session at the First Annual Canadian Oncology Nurses Association Conference in Vancouver in October 1988.

Quality assurance is an area of development in Outreach. In 1988, our data manager developed audits on the accrual mechanism and dictation quality. We have seen a great improvement in the quality of information we are receiving from our centers, and have continued to increase the numbers of patients treated within the program.

Our future goals

Two Outreach team members are conducting a research study on survival and disease-free survival in the Outreach Program. The study will be presented at the Canadian Psychosocial Conference in Vancouver in 1989. We hope to do more research in our program to evaluate the efficacy of Outreach in cancer patient management.

The area of quality assurance is one we plan to expand in the coming year. We plan to use our new pharmacy documentation and nursing standards to evaluate the performance of each individual center. We are also in the process of developing standardized treatment guidelines for our Outreach physician. Audits, based on these standards, will be done in conjunction with our annual visits to the centers.

More work is planned in the areas of evaluation of the nurses and physicians orientations to ensure that these Outreach health professionals have had adequate preparation for their roles in the community. A training program for Outreach pharmacists will also be developed.

The progress of this program would not be possible without the assistance of Manitoba Cancer Treatment and Research Foundation oncologists and radiotherapists, nursing and radiotherapy staff at both Manitoba Cancer Treatment and Research Foundation and St. Boniface General Hospital; Manitoba Cancer Treatment and Research Foundation administrative staff; Records and Registry, Information Services and Clinical Investigations Office staff; the Nursing Research Institute of U of M, and the Health Science Center Nursing and pharmacy staff; but most importantly all Outreach Center staff. All of these health professionals have played an important role in ensuring our program achieves its goals.

MEDICAL PHYSICS

DIRECTOR — P. Dunscombe, Ph.D., F.C.C.P.M.

PHYSICISTS

J. Bews. Ph.D. (from April 1/88); G. Froese, Ph.D., F.C.C.P.M.; W. Huda, Ph.D., F.C.C.P.M.; T. Lee, Ph.D., F.C.C.P.M. (to January 25/88); Y. McFarlane, M.Sc. (from July 1/88); R. Palser, Ph.D., F.C.C.P.M.; E. Papiez, M.Sc.; G. A. Sandison, Ph.D., M.C.C.P.M.; S. Shalev, Ph.D.; A. Sourkes, Ph.D., F.C.C.P.M.

TREATMENT PLANNING/SIMULATION/DOSIMETRY

L. Bailey, RTT; M. Carey, RTT; K. Fox, RTT (Feb. 29-Nov. 4/88); J. Grestoni, RTT (May 24-Aug. 31/88); B. Hinz, RTT; S. Iftody, RTT (from May 9/88); S. Ryder, RTT (from Oct. 31/88); N. Saunders, RTT (to May 20/88); M. Stewart, RTR, ACT; K. Suderman, RTT;, O. Werner, RT(NM); D. Willits, RTT; C. Zeller, RTT

MEDICAL DEVICES/MOULD ROOM

D. Bradley, R. Gallant, B. Griffiths, J. Legal, E. Maisey, R. Norton, I. Paul (from April 6/88), A. Wolk

NUCLEAR ELECTRONICS

V. Goertzen, C.E.T., M. Goldie, C.E.T., M. Hanuschuk, R. Shabaga, W. Stepaniuk

RADIATION PROTECTION

E. Cowdrey, M.Sc. (from February 1/88), R. Kowaluk, RTR; C. Neduzak, RTR; G. Philippot, RTR; J. Sandeman, B.Sc.

RESEARCH

S. Cosby, B.Sc., R. M. Das, Ph.D., K. Miskiewicz (Feb. 1-July 1/88); L. Papiez, Ph.D. (from May 2/88); David Viggars, Ph.D.

GRADUATE STUDENTS

J. Bews, Ph.D., T. Chu, M.Sc., K. Leszczynski, Ph.D., D. Lowe, M.Sc., Y. McFarlane, M.Sc., J. McLellan, M.Sc., M. Mirzai, M.Sc.; D. Savoie, B.Sc., P. Therrien, M.Sc., I. Yeung, M.Sc.

SUMMER STUDENTS

J. McLellan, Y. Patel, B. Sargeant

SECRETARIES

T. Davidson, G. Levesque (March 28 - June 30/88), M. Mead (from Nov. 16/88), B. Swayze

1. INTRODUCTION

1988 saw a modest increase in staffing levels as an acknowledgement of the increasing work load in all areas of clinical support. There remain a few sections within the Department which continue to face difficulties meeting the clinical demands placed upon them and solutions in these areas are being actively sought.

In Radiotherapy Physics much effort was absorbed in the preparation for the extensive upgrading of treatment facilities both at the M.R. MacCharles Unit and, more recently, at St. Boniface General Hospital. A high level of specialized support continued to be offered in the production of treatment plans, treatment aids and consultation in particularly difficult or unusual cases. The Radiation Protection Section consolidated its activities during 1988 as consequence of recent changes in its mandate. To the primarily health related facilities for which it retains responsibility a high level of service continued to be furnished. With the installation of increasingly complex imaging equipment the demands placed on the Section of Medical Imaging grew in both number and diversity. Again in 1988 members of this Section assisted the Radiology community in the selection, acceptance testing and ongoing quality control of a wide variety of equipment. Almost entirely due to the efforts of the staff in Medical Devices and Nuclear Electronics, radiation therapy and nuclear medicine equipment within Winnipeg continued to give reliable and safe service during the year. Partly in preparation for the impending installation of additional and replacement radiotherapy treatment machines, the computing facilities of the Department have grown. Clearly all members of the Department are becoming increasingly dependent upon such facilities to perform both service and academic functions.

A high level of teaching activity continued throughout 1988. The Department is involved in the training of medical physicists, residents in radiation oncology, nuclear medicine and radiology and radiotherapy technologists. In addition a variety of less extensive contributions are made to other groups of students.

In order to ensure that the Department continues to be able to offer state of the art clinical support a number of research and development projects are underway. These together with the other activities of the Department are summarized in the Sections which follow.

2. CLINICAL SUPPORT

RADIOTHERAPY PHYSICS

G. Froese

The Section continued to provide physics support for external beam therapy and for brachytherapy. A major review of the quality assurance program for the treatment machines and for the accessory equipment and also of the safety aspects of the operation of the machines was undertaken in 1988. As part of the over-all safety program an inservice for the therapy technologists is being conducted annually. An external check of our machine calibrations was provided in 1988 by a visit from the Radiation Physics Centre, Houston.

Rebuilding and shielding of the treatment room for the newly purchased high energy accelerator was started in 1988. In view of more recent information minor changes had to be made to the design of the lead shielding. In the preparation for the commissioning of the new machine for the acquisition of the required machine data a "Therascan" dosimetry system was obtained from AECL. The equipment has been tested by checking the data for our other machines. Preliminary discussion begun in 1988 regarding the installation of a high energy linear accelerator at the St. Boniface Hospital. The initial discussions dealt with the requirements for space, peripheral equipment and obtaining the approval by AECB of the building plans.

The Theratron F cobalt unit required a source change in 1988. The new source was acceptance tested and the unit recalibrated.

A new version V4A of the "Theraplan" computer system was installed. This required the re-entry of all machine data into the new version. The entry of the data for electron beams proved to be particularly time consuming.

Initial preparations were made for a procedure of whole body irradiation in conjunction with a proposed Bone Marrow Transplant program. A visit was made by a physicist to the Department of Therapeutic Radiology of the University of Minnesota to investigate the techniques used at that centre. The aim of the initial study was to determine the options available with our therapy equipment.

Members of the section contributed to treatment planning seminars and participated in many joint Physics/Radiation Oncology sessions.

MEDICAL IMAGING

R. Palser

The Medical Imaging Section provides a clinical support service to the nuclear medicine departments of all Winnipeg hospitals and to the radiology departments of the Health Sciences Centre (HSC) and the St. Boniface General Hospital (SBGH), the two teaching hospitals. The activities of the Section cover the areas of equipment evaluation, recommendations regarding the purchase, acceptance testing, optimal use and ongoing quality control, developmental research, radiation protection and teaching. In addition some special projects are undertaken for other provincial hospitals.

At the HSC nuclear medicine department a single photon emission computed tomography (SPECT) gamma camera and its associated computer system was evaluated for inclusion in the currently operating network, tendered and purchased for delivery in 1989. At Brandon General Hospital a mobile gamma camera with clinical computer was evaluated and purchased. A second mobile system for SBGH was approved for purchase late in 1988.

In the nuclear medicine development area, work has continued on the radiopharmaceutical compartmental modelling project, a comprehensive and automated SPECT quality control program is near completion and will be integrated into the ongoing quality assurance program. A number of clinical protocols were reviewed and modified to make better use of new and updated equipment in the various departments.

In the radiology departments, at SBGH the performance characteristics of cardiovascular angiography equipment were evaluated and tenders for such a system reviewed; at the HSC a computed tomography (CT) scanner and a digital angiography X-ray unit were acceptance tested and their performance assessed; also a lithotripter, an ultrasconic shockwave generating device used to smash renal stones in situ, was installed and acceptance tested. At Brandon General Hospital their computed tomography scanner was acceptance tested and an evaluation of specific CT scanners made for the Manitoba Hospital Services Commission.

Several reports and papers have been written on estimation and comparison of radiation doses and risks from various radiological modalities. This work has enabled a better comparison of the radiation doeses and consequent health risks to patients, hospital staff and the population at large.

The Nuclear Magnetic Resonance (NMR) work reported last year has continued with additional site visits, scientific meeting participation, supplier contact and involvement in an NMR research project. Equipment evaluations for the purchase of an NMR machine by SBGH have been performed and test devices constructed for measurement of the performance parameters.

The nuclear medicine quality control program continues to monitor the performance of all clinically used gamma cameras, uptake probes, radiation monitoring equipment, well counters and some film processors in the city hospitals. Review of each piece of equipment enables it to be maintained in long term optimal and stable condition and comparison with newer equipment aids in the scheduled replacement of older units.

COMPUTER APPLICATIONS

S. Shalev

The treatment planning computer has been upgraded to permit more accurate and efficient preparation of treatment plans. It now has two work stations, increased storage capability and improved display and plotting accessories. Three-dimensional treatment planning has been implemented, using CT scans to obtain the required anatomical information, and employing dose volume histograms for the comparison and evaluation of alternative plans.

A comprehensive program is underway to improve the precision of treatment delivery, and to verify the accuracy of patient positioning during treatment. A digital computer has been installed in the department for viewing portal films, using a variety of image processing techniques to improve the quality of the images. Additional software is under development to permit the quantitative determination of treatment accuracy by comparing simulator and portal films on a routine basis. In addition, an on-line portal imaging system has been developed and installed on the 4 MV linac therapy unit. It is used for the display of patient location during treatment and is undergoing clinical testing and comparison with the conventional use of portal films.

The Section has carried out a number of developmental projects in collaboration with commercial companies, both in Canada and abroad, with the goal of having hardware and software developed in our department distributed on a world-wide basis to other cancer centres.

TREATMENT PLANNING/SIMULATION

M. Stewart

The treatment planning and simulator Section is responsible for providing technical support for the individualized design and implementation of treatment plans for the treatment of cancer with radiotherapy.

During the year A.E.C.L. Therasim was used full time. The Picker simulators at the Manitoba Cancer Treatment and Research Foundation and the St. Boniface General Hospital were used approximately 2.5 days per week until October. With an increase in staff during November it was then possible to operate 2 simulators full time. The total number of simulations performed at the Manitoba Cancer Treatment and Research Foundation was 2,691 and at the St. Boniface General Hospital was 525. The combined total is 3,216. This represents a decrease of 4% over last year.

The method of acquiring patient statistics has changed this year in order to make use of the Workload Measurement System (WMS). In previous years any patient requiring even the simplest of calculations or the reading of one port film was included in the total treatment planning patient count. The WMS is still in the testing phase for all the treatment planning procedures but there are assigned numbers of units for each procedure. Ultimately, WMS will be useful in determining appropriate staffing levels.

Patients come to treatment planning for contours, plans, lead compensators, aluminum compensators and the design of cerrobend blocks for field shaping. The number of patients requiring one or more of these procedures was 789 as compared to 782 for 1987. Contours totalled 436; plans and distributions 464; lead compensators 102; aluminum compensators 29; design of cerrobend blocks 326. In addition to these procedures, plates for design of cerrobend shielding using standard blocks totalled 1,221; port films taken on the machines to verify accuracy of patient positioning totalled 922; clinical TLD measurements totalled 89. Dosimetry of gynecological cesium insertions has been calculated on 18 patients.

In November, an upgraded treatment planning system was installed, resulting in faster computations, color coded plots of treatment plans and no loss of computer time due to plotting. There are 2 terminals to permit 2 users at the same time. With this computer, it is expected that treatment planning will be able to meet the increased demand required with the installation of new treatment machines.

NUCLEAR ELECTRONICS

W. Stepaniuk

The Nuclear Electronics Section of five technologists continues to provide equipment service and preventative maintenance to Radiotherapy and Nuclear Medicine centres in Winnipeg. These centres are the Manitoba Cancer Treatment and Research Foundation, Health Sciences Centre, St. Boniface Hospital, Grace, Victoria, Misericordia and Seven Oaks general hospitals.

The workload of this Section continues to increase annually, with major equipment purchases, increased requests for support services and more involvement in development work. We have been asked to supply two additional automatic radioisotope dispensing devices for the Radiopharmacy Lab; also another Molybdenum Technetium Generator has been requested. With the installation of the new Siemens accelerators to take place in 1989 an additional electronic technologist will join our staff. With future equipment purchases, additional staff, increased budgetting for spare parts and test equipment, the Nuclear Electronic Section will continue to provide fast and efficient equipment service and preventative maintenance to Radiotherapy and Nuclear Medicine centres in Winnipeg.

Performance of Radiotherapy and Nuclear Medicine Equipment in 1988 was an follows:

1. The AECL Theratron 780 Co^{60} and the Picker Therax Simulators at St. Boniface General Hospital continued to provide good service with no major treatment interruptions.
2. The Siemens 250 kV X-ray and the Chaoul Therapy units at the Manitoba Cancer Foundation continued to give dependable service with only minor interruptions.
3. The Theratron F Co^{60} at the Manitoba Cancer Foundation was removed from service for 2 days to have the source replaced in the unit and the shutter overhauled by Atomic Energy of Canada.
4. The Picker Therax simulator still provides good service. The A.E.C.L. Therasim 750 simulator had its rotating anode X-ray tube replaced due to a cracked exit window.

5. The 4 MV SHM Linear Accelerator had no major parts replaced or breakdowns.
6. The Saggittaire Linear Accelerator which is operating 16 hours per day continues to provide good service. During a scheduled maintenance day a crack was noted in the machine's gantry. The repair was carried out by Bristol Aerospace on the weekend so as to keep the treatment time interruption to a minimum. Due to the Sagittaire's heavy workload, the unit is to be removed from service for an overhaul once the new Siemens accelerators are put into service.

   The performance of Nuclear Medicine equipment and new purchases is as follows:

   (a) The Nuclear Medicine Department at St. Boniface General Hospital had no major breakdowns during the year. A new Elscint SPECT gamma camera and computer were installed at the beginning this year.

   (b) Nuclear Medicine equipment at the Health Sciences Centre experienced no major breakdowns with only minor interruptions during the year. The same can be said for Grace, Victoria, Misericordia and Seven Oaks general hospitals. Only one major piece of equipment was budgetted for the Health Sciences Centre, that being a new Elscint SPECT gamma camera and computer.

MEDICAL DEVICES

J. Legal

Three major projects occupied the bulk of our developmental efforts.
- A custom quadriplegic wheelchair
- A newly designed technetium generator
- Two semi-automated dispensers for radiopharmaceuticals.

These devices are described under Section 5 of the Department of Medical Physics Annual Report.

Other developmental work undertaken by Medical Devices includes:

— A modified hydraulic stretcher allows patients in a breast study to be gently lowered over a calibrated water reservoir which is used to accurately measure breast volumes.

— Based on an earlier design a heavy duty stand incorporating many degrees of motion is used to position custom shaped lead shields in virtually any area between the patient and teletherapy unit.

— Young patients normally confined to respiratory wards can now be ventilated and monitored for several hours from a mobile self contained unit, making it possible for staff to take patients on outings outside the hospital. Three units were built.

— A motorized accessory for our Tungsten Inert Gas — T.I.G. welder has proven very useful in obtaining excellent joints in stainless steel vessels and other parts fabricated in the shop.

— For radiation treatment of the lower lip a reuseable applicator was designed to position iridium wire sources inside and outside the mouth. The patient bites down on a fitted denture type block to ensure repeatable positioning.

Other activities included:

— The fabrication of specialized equipment for ongoing research projects in the areas of portal imaging, hyperthermia and CT xenon studies.

— Coordinating fibre glass repairs to the Sagittaire gantry by Bristol Aerospace who performed $2,000.00 worth of work at no cost to the Foundation.

— Participation in developing floor plans for renovations to the Radiation Oncology Clinic — presently under construction.

— Assisting the Department of Radiology in a major upgrade of their diagnostic chest x-ray unit.

— Upon request from the Cancer Control Agency of B.C., drawings of our mantle treatment system were upgraded and sent to them.

The number of patients referred to the Mould Room for fabrication and fitting of custom "Uvex" moulds has been consistently recorded for the past 8 years. In 1981, 708 patient visits were recorded, by 1988 the number has increased to 1,270 patient visits. Although detailed statistics on other appliances and related services have not been as diligently recorded in the past we are certain that production increases in these areas have been just as dramatic.

In 1988, 631 patients were fitted with "Uvex" shells. It may be of interest to realize that in the process 9,900 ft. of plaster bandages, 10,750 lbs. of plaster and 60 sheets of plastic, at $100.00 per sheet, were consumed. 533 patients had custom shield casts of the low melting point alloy cerrobend, which required approximately 15,000 lbs. to be melted and poured into moulds. At $9.00 per lb. it is fortunate that most of this material can be recycled. 121 patients were fitted with lead masks or other small shields; posterior triangle apertures were fabricated for 63 patients and wax boluses were moulded for 185 patients. Other devices fabricated mainly by vacuum forming techniques were breast positioning plates for use in radiology, training mannequins for educational purposes, A.B.S. components for wheelchairs, oxygen cylinder mounting holsters for the Department of Respiratory Therapy Operating Room and other users, iridium applicators and a custom hand prosthesis for a burn victim. Mould room staff are also responsible for the storage, monitoring and delivery of sealed sources for brachytherapy.

3. RADIATION PROTECTION

A. M. Sourkes

In 1988 the Radiation Protection Section (RPS) continued to administer the MHSC-Contract specified portion of the X-Ray Safety Regulation under the Public Health Act (C.C.S.M.c.P210) which was bilingualized and metricized to become MR341/88 R in August. According to revised contract terms the RPS ceased provision of environmental radioactivity related consulting services to and on behalf of the Workplace Safety and Health Department and Environment Department and similarly ceased the provision of radiation incident emergency response services.

Under the X-Ray Safety Regulation, the major effort of the three qualified inspectors consisted of the survey of medical, dental, chiropractic, and educational X-Ray units throughout the province. Included in the survey effort was the annual mail out, radiation dose measurement evaluation of 636 dental X-ray units. The RPS also continued to serve as the intermediary for the personnel radiation monitoring service in use by all contract related X-ray user groups. In the area of non-ionizing radiation protection a total of 429 device inspections were carried out by the two qualified officers in that area. Device-types covered included those emitting potentially hazardous levels of ultra-violet light, microwaves, radiofrequency radiation, contact ultrasound, and coherent visible or infrared laser light, present in medical, paramedical, or public access locations. In addition assistance was given in the proper disposal of twenty-one radioactive sources prior to April 1, 1988 after which time consulting services changes no longer permitted inclusion of this type of activity. A complete summary of all activities is tabulated below.

SUMMARY OF ALL 1988 RADIATION PROTECTION ACTIVITIES

Activity	Number
Protective Barrier Room Design-Specification Written-Approvals	119
Protective Barrier Installation Location-Inspections	45
Dosimetry Exposure Investigations	11
Wipe Sample Analysis	284
Response to Public Inquiries	438
Radiation Safety Lectures	14
Mail-In Dental Unit Checks	636
Non-Ionizing Device Surveys	429
X-Ray Machine Inspections	492

SUMMARY OF 1988 X-RAY MACHINE REGISTRATION AND INSPECTION DATA

Type of Installation	Total Registered	In Service	Surveyed in 1988	Approved Initially	Corrected During Survey	Approval Withheld	Approved Subsequently
Chiropractic	41	38	25	15	0	10	10
Dental	887	884	202	171	5	26	16
Educational	58	53	9	7	0	2	2
Hospital	173	163	93	90	0	3	3
Lab & X-ray	134	132	123	106	1	16	16
Medical Office	74	73	40	39	0	1	1
Industrial	31	31	0	0	0	0	0
Veterinarian	85	85	0	0	0	0	0
Totals	**1,483**	**1,459**	**492**	**428**	**6**	**58**	**48**

SUMMARY OF 1988 NON-IONIZING RADIATION INSPECTION ACTIVITIES

SURVEY AND LOCATION TYPE

(A) HOSPITALS AND CLINICS

Inspection Device Type	Number Inspected	Approved Initially	Corrected During Survey	Approval Withheld	Approved Subsequently
Lasers	2	1	1	0	0
Microwave	23	23	0	0	0
Radiofrequency	15	2	12	1	1
Ultraviolet	23	20	2	1	0
Ultrasound	68	45	10	13	11
Other	4	4	0	0	0

(B) PARAMEDICAL AND PUBLIC HEALTH

Lasers	13	2	8	3	3
Microwave	0	0	0	0	0
Radiofrequency	3	0	3	0	0
Ultraviolet	153	35	73	45	9
Ultrasound	121	71	23	27	13
Other	4	4	0	0	0
Totals	**429**	**207**	**132**	**90**	**37**

4. ACADEMIC ACTIVITIES

As part of the graduate programme in Medical Physics offered through the University of Manitoba 3 credit hour courses were delivered in both Diagnostic Imaging and Medical Radiation Physics. As in previous years these courses attracted a relatively high enrolment. In the Fall of 1988 a new course, Seminars in Medical Physics, was offered to provide Ph.D. students the opportunity to study selected topics in Medical Physics to a depth not possible in the regular didactic course. The success of this approach remains to be assessed. During 1988 three students successfully completed their studies (J. Bews, D. Lowe and Y. McFarlane) and three students (K. Chantziantoniou, J. McLellan and M. Mirzai) joined the program. One student (D. Savoie) withdrew.

Residents in primarily Radiation Oncology and Nuclear Medicine received teaching on a tutorial basis from members of the Department throughout the year.

The intake of Radiotherapy Technology students was larger in 1988 than in previous years due to the participation of two students from Saskatoon. The increased numbers required some alteration of the organization of laboratory classes.

With the ubiquity of microcomputers many members of the Department and elsewhere in the Foundation expressed the desire to achieve instruction in the use of such devices. In the absence of a suitable locally offered course several members of the Department designed and delivered a series of classes to interested individuals. These appear to have been very successful.

In addition to the fairly extensive involvement in major teaching programs outlined above a variety of seminars and talks were delivered by the staff to audiences both within and outside the Foundation. The Medical Physics seminar series continued to attract a wide range of good speakers and high attendance levels.

5. RESEARCH AND DEVELOPMENT ACTIVITIES

QUANTIFICATION OF RADIOTHERAPY TREATMENT PLANS

S. Shalev, D. Viggars, P. Therrien, P. Hahn

We have continued our close collaboration with Theratronics International Limited on the development of computer programs for the quantitative evaluation of alternative treatment plans. Images of regret and score functions are used for two-dimensional plans, and for volumetric (3-dimensional) plans we employ dose volume histograms, histograms of regret and volume shift histograms. Multiple CT slices are used to define the patient's anatomy, and to delineate the target volume and any radiosensitive organs which must be shielded from the radiation. Dose prescriptions are prepared for each patient, and interpreted as constraints on the acceptable shape of the dose volume histogram. These techniques permit the evaluation of complex three-dimensional dose distributions in a simple, quantitative and reproducible manner, and will facilitate the use of three-dimensional planning on a more routine basis.

PORTAL VERIFICATION

S. Shalev, K. Leszczynski, T. Chu, S. Cosby, L. Rsinstein, A. Meek**
**Stony Brook University Hospital, NY*

A Portal Film Enhancement Station, known as PEST, has been developed in collaboration with the State University of New York at Stony Brook. It acts as an "electronic view box" and allows the technologist to view low contrast portal films with improved accuracy, without the need for reduced room lighting. An automatic method of comparing portal and simulator films is under development for verifying the accuracy of treatment.

An on-line fluoroscopic portal imaging device has been developed and installed on one of our therapy machines. It provides a live image of the patient during treatment, and permits the identification of any localization errors while the treatment is in progress. It is undergoing extensive clinical testing to determine the optimal way of integrating it into routine clinical practice.

The on-line portal imaging system provides data, for the first time, on the extent of patient movement during radiation treatment. These data are being used in a study of the dosimetric implications of organ movement, with the goal of modifying planning procedures to take this effect into account at the planning stage.

FIELD PLACEMENT ERRORS IN RADIOTHERAPY

P. B. Dunscombe, K. Fox and S. Ryder

A detailed study of the precision with which field placement errors can be quantified from portal films of pelvic fields has been completed and is now in press. The extension of this work, which is currently being pursued, is directed towards the identification of the origin of observed errors. Only with such information can consistent remedial measures be instituted. A framework has been developed to permit the classification of field placement errors and this is currently being assessed for applicability in the clinic.

EXPERIMENTAL HYPERTHERMIA OF THE SPINAL CORD OF THE MOUSE

G. Froese, P. B. Dunscombe and R. M. Das

In therapy with radiation or hyperthermia the spinal cord is often a dose limiting tissue. We have investigated the effect of heating 12 mm of the thoraco-lumbar spinal cord of C3H mice. From our previous investigation of different heating techniques, i.e. heating with waterbath alone, with a waterbath-radiofrequency (rf) combination and rf-heating alone with dorsally located electrodes we concluded that rf alone best spares adjacent visceral and superficial tissues. The temperature of the spinal cord was monitored by measuring the temperature at a point located dorsal to the spine. Three groups of 9 mice were heated for 1 hour to 41.5°C, 42.5°C and 43.5°C respectively. Observable neurological damage was seen in some mice of all groups as early as one day after treatment. The impairment of the leg extension reflex when the mouse is lifted by its tail was measured by observing the video-recorded leg extension and calculating the percent reduction in the leg extension (RLE) after treatment. A RLE of 40% corresponded to overt paralysis and 90% of the animals in all temperature groups with a RLE of 40% or more died within 5 days after treatment. Of those animals which survived for 8 weeks some showed minor symptoms on the 14th day from which there was a partial recovery after 8 weeks. The ED_{50} for a RLE of 40% or more (and also the LD_{50}) was 42.9°C. The rapid response of the spinal cord and the high sensitivity of the cord will have to be taken into consideration in the clinical application of hyperthermia.

THE MEASUREMENT OF REGIONAL CEREBRAL BLOOD FLOW USING XENON ENHANCED COMPUTED TOMOGRAPHY (Xe/CT)

J. Bews, P. B. Dunscombe, R. Palser, M. Mirzai, B. McClarty and K. D. Jones

Local Cerebral Blood Flow (LCBF) and partition coefficient (1) can be measured indirectly by monitoring the uptake of Xenon in brain tissue during patient inhalation of the inert gas. Our research is currently aimed at quantifying the errors associated with the clinical application of the Xe/CT technique. Of particular interest are the limitations imposed by quantum noise, an unwelcome component of all CT scans, on one's ability to accurately monitor Xenon accumulation and hence determine flow. In this study, errors are examined using Monte Carlo based computer simulations in which the Xe/CT technique is modelled on an IBM personal computer. Steps have also been taken to implement the Xe/CT technique in a clinical study of LCBF in the vicinity of glioblastoma. The required apparatus has been assembled and preliminary calibration measurements performed. Patient studies will begin in 1989.

A parallel project has been established to study the feasibility of measuring regional cerebral blood flow with the radiopharmaceutical TC-99m-HMPAO. This agent crosses the blood brain barrier, is trapped in the brain tissue, and can be visualized using a single photon emission computed tomography (SPECT) system. Although this technique has some theoretical limitations related to the radiopharmaceutical kinetics and quantification of the amount of labelled tracer in the brain tissue, its major advantages are that three dimensional measurements are possible and that the clinical procedure is almost non-invasive.

The SPECT gamma camera at the Health Sciences Centre has been used to develop empirical methods to predict the amount of tracer in brain phantoms from external measurements. A computer program has been written to simulate the radiopharmaceutical trapping process and various models are being compared using washout data taken from the literature.

ELECTRON DOSIMETRY

G. A. Sandison, D. Savoie, L. Papiez, W. Huda, E. Papiez, J. McLellan

A project for improving radiation dose calculation accuracy in cancer patients being treated with electrons is on-going and has recently attracted National Cancer Institute of Canada funding. Dr. Lech Papiez joined the research group as a post-doctoral fellow and Mr. John McLellan as a M.Sc. student. Theoretical development of a new calculational model for electron dose in tissue has shown substantial and rapid progress during 1988. Currently this model is being implemented as a computer algorithm on the LSI treatment planning computer.

BIOMEDICAL NMR

W. Huda, J. Peeling, G. Froese, J. Bews

Considerable effort has been put into the selection of Nuclear Magnetic Resonance equipment which is to be acquired by the Health Sciences Centre and St. Boniface General Hospital. This includes the design and manufacture of phantoms to evaluate commercially available NMR equipment. Work is also being performed on a small bore NMR system in Ottawa using rats to study the effect of ischemia, and the quantification of the observed changes is being undertaken.

LOW OSMOLALITY CONTRAST AGENTS

W. Huda, J. B. Sutherland

This work was undertaken to evaluate the financial costs incurred through the introduction of low osmolality contrast agents into diagnostic radiology and compare these with the "benefits" to be obtained in terms of lower mortality and morbidity rates. The conclusions reached showed that the cost of saving a life by the introduction of low osmolality contrast agents were much higher than other *medical* practices, but comparable with societal activities (e.g. improvements in road safety) and with radiation protection practices.

NUCLEAR MEDICINE DOSIMETRY

W. Huda, G. A. Sandison, K. Gordon, I. D. Greenberg

A number of studies have been undertaken to quantify the radiation doses received by patients undergoing diverse nuclear medicine studies. Special emphasis has been given to patients undergoing thyroid studies. In addition, a new method of determining the values of effective dose equivalents in Nuclear Medicine and in Positron Emission Tomography has been finalized and is in the process of being published.

DIAGNOSTIC X-RAY DOSIMETRY

W. Huda, G. A. Sandison, J. Bews, A. M. Sourkes, R. F. Palser

Considerable effort has been applied to produce radiation dose estimates to patients undergoing a number of diagnostic X-ray examinations in Manitoba. Examples of these studies include chest X-ray examinations, chiropractic examinations which use X-rays, lithotripsy procedures and CT studies. The results of these investigations are currently in the process of being published in the scientific literature.

OCCUPATIONAL DOSES IN RADIOTHERAPY

W. Huda, J. Bews, A. M. Sourkes

A detailed investigation was undertaken of the occupational radiation doses received by staff in radiotherapy (including brachytherapy nurses) in Manitoba for the period 1980-1986. The study examined the significant trends in radiation exposures over this period, and highlighted the main contributors to occupational doses in radiotherapy.

RADIATION PROTECTION

W. Huda, K. Gordon, S. Boutcher

A number of studies have been undertaken to improve radiation protection in the areas under the Clinical Isotope Committee. These include an analysis of the utility of Nuclear Medicine technologists wearing lead aprons, and the radiation protection problems associated with a new treatment modality which uses Yttrium-90 microspheres to treat liver metastases.

MAMMOGRAPHY RADIATION DOSIMETRY

W. Huda, A. M. Sourkes

The female breast is one of the most sensitive organs to radiation induced cancer. The advent of "screening" has highlighted the concern of the radiation doses associated with X-ray mammography. This study is designed to show the trends in the individual and collective radiation doses associated with mammography in Manitoba for the period 1980-1988.

CUSTOM QUADRIPLEGIC WHEELCHAIR

J. Legal, R. Gallant, A. Wolk

This project was undertaken with the cooperation of Otto Bock Orthopedic Industries of Canada Ltd. and other specialists to accommodate the special needs of a quadriplegic patient with a spinal cord injury at the C1-C2 level. State of the art technology was employed to produce a form fitting motorized reclining seat which hopefully will alleviate recurring problems that have plagued the patient for several years. A battery operated ventilator sustains breathing while a complex alarm system, developed by Biomedical Engineering, monitors potential respiratory problems. The chassis features an articulating front suspension with low pressure, high volume tires which help to minimize drive friction over uneven soft terrain while maintaining a comfortable ride for the patient. We believe this chair with all its features is lighter and more compact than any comparable design and we are pleased to report that it has been enthusiastically accepted by the user.

DISPENSING RADIOPHARMACEUTICALS

J. Legal, R. Shabaga, R. Gallant, A. Wolk

Mentioned in the annual report for 1987 was the development of a prototype machine designed to pump a preset volume of liquid radioisotope from a reservoir to smaller hermetically sealed vials. The main purpose of this device is to reduce the radiation dosage to personnel in the radiopharmacy, but it has also been found to be more precise in volume selection than manual methods. It has been extensively tested and is now accepted as a practical instrument. As a consequence we have received a request for two additional units which are presently nearing completion. This newer model will incorporate a microprocessor to control the motors and valve which can pump and dispense a range of radioisotopes inside a shielded housing. A lead glass window allows the operator to visually monitor the process in safety.

TECHNETIUM PRODUCTION

J. Legal, M. Billinghurst, R. Palser

Technetium is a radiopharmaceutical used in approximately 90% of all diagnostic procedures in nuclear medicine. Due to its short half life it must be produced every day from a longer lived isotope, usually some form of molybdenum, which in turn can be purchased from drug companies employing powerful reactors. Since the early seventies the Radiopharmacy Laboratory at the Health Sciences Centre has employed a method of producing technetium different than other centres. Our process is somewhat more elaborate and requires a relatively complex machine which we have developed and produced here but overall costs are less and it is estimated that over the years substantial savings have been realized. To date we have built 4 units which supply most of the needs of the province. A fifth unit, nearing completion, has more shielding to comply with stricter radiation protection standards and is designed to process a larger volume of a low specific activity molybdenum which can be produced by many small low power reactors. This capability has attracted the attention of Atomic Energy of Canada Limited who have indicated their interest in promoting and marketing this machine worldwide.

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EPIDEMIOLOGY AND BIOSTATISTICS

DIRECTOR — N. W. Choi, M.D., M.P.H., Ph.D., F.A.C.E.

BIOSTATISTICIANS — N. A.Nelson, B.A., M.A., Ph.D.;
P. F. Moodie, B.Sc. Hons., M.Sc.

SECRETARY

M.-P. Regan

RESEARCH FELLOW

H. C. Oh, M.D., M.P.H., DR, P.H.

RESEARCH ASSISTANTS

J. Du, J. Ediger

FIELD INVESTIGATORS

S. Cormack, C. Sobie, J. Stasiuk, C. Strutt

DATA PROCESSING

M.-P. Regan

Introduction

In 1968, the program of Epidemiology and Biostatistics was established in the Manitoba Cancer Treatment and Research Foundation with a view to furthering the establishment of preventive measures against cancer and to facilitating data storage and retrieval systems in the registries of cancer patients and cytology screening for epidemiological, statistical and evaluation studies. The program was one of the first of its kind in Canada and has resulted in significant contributions to the cancer control programs of the province.

The provincial registries of cancer patients and cytology screenings have been primary sources of epidemiological studies and have been steadily improved over the past two decades. Studies on the interaction of genetics and environmental factors became an added component of our program since 1985.

The Epidemiology and Biostatistics program has also been active in undergraduate and graduate teaching programs.

While the Director of this department has been actively engaged in international collaborative activities over the years, in recent years, he has also been active in consulting with the World Health Organization on behalf of a number of governments on cancer prevention and control.

The following report outlines the progress of the ongoing projects and briefly describes the nature of the new studies.

STUDY OF LUNG CANCER AND DOMESTIC ENVIRONMENT

N. W. Choi, N. A. Nelson, H. C. Oh, J. Du, C. Sobie, C. Strutt, J. Stasiuk

As we reported in our 1987 annual report, we are conducting a case-control study of lung cancer and domestic environment. We have been conducting this project in close collaboration with the Health Protection Branch of Health and Welfare Canada.

The project consists of interviewing subjects using a standard questionnaire and documenting their life history regarding smoking, exposure to occupational risk factors, previous residences as well as many other variables of interest.

So far, we have interviewed 600 pairs (cases and controls) and obtained grab samples of radon in their present homes.

We have started on the next phase of this study involving tracing subjects previous residences and obtaining the permission of the present resident to place dosimeters in his/her home for a period of one year.

We are proceeding with the coding and computer inputting of the questionnaires and this project is progressing well.

PASSIVE SMOKING AND LUNG CANCER

H.C. Oh and N. W. Choi

Currently there is an increased interest regarding the role of involuntary smoking in the etiology of lung cancer among non-smokers. The 1986 Surgeon General's report in which the subtitle "The Health Consequences of Involuntary Smoking" concludes that involuntary smoking is a cause of disease, including lung cancer in healthy non-smokers. A review recently published by the National Academy of Sciences states that approximately 20% of the estimated 12,200 lung cancer deaths occurring annually in the United States are attributable to environmental tobacco smoke. This means involuntary smoking has some effect on lung cancer risk in non-smokers and mild and moderate smokers. We are not only interested in the effect of involuntary smoking on non-smokers but also on mild smokers. That is, lung cancer risk should be assessed in relation to both involuntary smoking volume and that of voluntary smoking in this study.

We have already started to collect data on known risk factors of lung cancer cases who come from the Manitoba Cancer Registry including past smoking and involuntary smoking in conjunction with our study on lung cancer and home environment. This is a community based case-control study using interview survey with a systematized questionnaire.

As a result of our effort, the Environmental Health Directorate of Health and Welfare Canada have shown an interest in the subject and are exploring the possibility of expanding this study to other centres in Canada. A multicentre pilot study is envisaged.

CANCER AMONG REGISTERED INDIANS IN MANITOBA

N. W. Choi, N. A. Nelson, P. F. Moodie, H. C. Oh, P. West, R. Musto

Our department is involved in a new in-house project involving the Medical Services Bureau of National Health and Welfare Canada.

Our first step in this study is to link the Medical Services Bureau's data base to the Manitoba Cancer Registry. This data base includes registered Indians who have resided in Manitoba at any time during a nine year period, 1978-1986. This data base includes some 60,000 registered Indians.

Linkage of the two data bases will identify those Indians who have been diagnosed with cancer during the study period. Calculation of expected numbers of various cancers, based on cancer incidence in non-Indian population of Manitoba will be done. Certain cancer sites selected based on excess/deficit will be further investigated by means of a case-control study. A standardized questionnaire will be used requiring the assistance of nursing station personnel.

CASE-CONTROL STUDY OF THYROID CANCER WITH EMPHASIS ON RADIATION AS A RISK FACTOR

*N. W. Choi, J. Ediger in collabortion with the C.C.R.E.R.G.**

As reported previously this is a national case-control study to assess the importance of medical irradiation in the induction of thyroid cancer.

Subjects are patients with thyroid cancer, newly diagnosed in Manitoba as well as across Canada. Sex and age-matched controls are selected randomly from the general population.

Data analysis will be carried out on a centre-specific and pooled bases.

This study is continuing in 1989.

*Canadian Cancer Registries Epidemiological Research Group.

EPIDEMIOLOGY STUDY OF DIET AND PANCREATIC CANCER

N. W. Choi, N. A. Nelson, P. F. Moodie in collaboration with the International Agency for Research on Cancer, Lyon, France

This project was initiated in 1983 with a series of pilot studies designed to ascertain the feasibility of obtaining data relating to lifestyle factors in the etiology of this disease.

Data collection has been finalized in all six collaborating centres (Toronto, Winnipeg, Montreal, Warsaw, Utrecht, Adelaide) and the final data base has been assembled in Lyon. Results of this study will be presented in the IARC Scientific Publications Series.

AN INTERNATIONAL STUDY OF BRAIN TUMOURS AMONG ADULTS. A CASE-CONTROL STUDY

N. W. Choi, N. A. Nelson, J. Ediger in collaboration with the International Agency for Research on Cancer, Lyon, France.

This is a case-control study designed to explore the relationship between brain tumour incidence and a variety of personal characteristics and exogenous exposures.

The study was initiated in 1986 and ten centres from around the world are participating. Data collection is progressing well and data verification is being assessed using a program written at IARC and distributed to the centres. To date, approximately 1,000 cases (from all centres) have been interviewed in this study with the appropriate number of controls.

Manitoba has so far contributed 120 cases and 163 controls to the data base.

Subject enrolment is expected to extend throughout 1989.

AN INTERNATIONAL STUDY OF BRAIN TUMOURS AMONG CHILDREN.

N. W Choi, N. A. Nelson, P. F. Moodie, J. Du in collaboration with the International Agency for Research on Cancer, Lyon, France.

This study is to evaluate the role of childhood exposure to N-nitroso compounds as well as other variables such as environment and parents' occupational exposures. We are also investigating the importance of two known etiologic factors: (a) in utero and childhood exposure to ionizing radiation, and (b) neurofibromatosis and other genetic syndromes which predispose patients to brain tumour development.

Winnipeg along with other centres is still ascertaining cases of brain tumours in children as reported in our 1987 annual report.

Manitoba has so far contributed 60 cases and 97 controls to the data base. The study is in the final stages of data collection and validation. Final results should be available early 1990 when all data are fully analyzed.

THE EFFECTS OF CHEMOTHERAPY ON SITES SUCH AS OVARY, TESTIS AND HODGKIN'S DISEASE AS IT RELATES TO SECOND PRIMARY CANCER. A CASE-CONTROL STUDY.

N. W. Choi, N. A. Nelson, J. Ediger in collaboration with the International Agency for Research on Cancer, Lyon, France.

Data collection for the case-control study of second malignancies was completed in the first half of 1988, and statistical analyses are well underway. Issues being explored in the statistical analyses include the relative carcinogenicity of different agents and combinations, the temporal relationship between therapy and second cancer risk, and the effect of other factors such as stage of first cancer, age and splenectomy on the risk of second malignancy. We have already clearly demonstrated the leukaemogenicity of five alkylating agents which are or have been used in ovarian cancer therapy.

The statistical analyses are continuing and should be completed shortly and results published in 1989.

BIOMETRY

N. A. Nelson and P. F. Moodie

We have been involved in two clinical trials and given assistance and consultation in a number of other projects. Meta analysis was provided for combining studies where the proportion surviving was the outcome variable. In this analysis the lengths of observations varied between studies. A considerable amount of software for comuter analysis has been developed. Because of this development we will be able to respond to requests from different geographical regions to give observed incidence, expected incidence, relative odds and results of tests of significance much more quickly. In addition, we will not need to burden the cancer registry with crosstabulations of observed cases, we will simply request a data file. Other software involves better diagnostics and examinations of fit for nonlinear regression models and tabular recoding with an algorithm for breaking combination codes.

An area of special interest for future endeavours is data base management, particularly the linkage of data files. This is a major aspect of cohort analysis. Another service that is being planned is the providing of tutorial sessions to residents.

Some previously reported projects have now been completed. The large simulation study for multivariate tests of variability has been completed and the results have been published.

Dr. Oh's assistance in our many endeavours has been greatly appreciated.

The following projects have now been completed and some are already published and the publication of other manuscripts is eminent.

- International study on radiation effects on second primary cancers — Phase II: Case-Control Study.
- Epidemiology of male breast cancer and survival after diagnosis.
- Does family history of breast cancer improve survival among breast cancer patients?
- Long-term survival among breast cancer patients.
- Childhood cancer is asociated with elevated cancer risk in parents.
- Risk factors for gastric cancer — a case-control study in the Republic of Korea.
- Some neonatal factors relating to childhood cancer.

PUBLICATIONS

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Musto, R. J., Choi, N. W. Linking Population Based Registries for Cancer Research Among Canadian Indians. Proceedings of the Third Annual Conference on Information Technology in Community Health. November 1988.

ONCOLOGY RECORDS AND REGISTRY

Director — H. Schipper, BS Sc, MD, FRCP(C)
Assistant Director — G. Hanson, CCHRA(A)

CENTRAL CANCER REGISTRY

Supervisor — J. Kostyra
Cancer Registry Officers — J. Walker, D. Timchishen, M. Parisien, L. Costa, K. Isaak
Death Clearance Clerk — R. Bresch
Admission/Separation Clerk — F. Shilshtut
Pathology/Cytology Processing Clerk — A. Cookson
Clerical Staff — R. Zaroda, C. Hildebrand

HEALTH RECORDS SERVICES

Supervisor — E. Tower
Intake Coordinator — S. Johnson
Records Processing Clerks — M. Hammerback, L. Harder
Records Control Clerks — C. Kelly, L. Arseniuk
Medical Transcriptionists — V. Tuckett, D. Meakin, D. Foster, M. Halischuk, K. Filbert
Interview Clerk — K. Whalen
Courier/Mail Services — M. Varkerti
Receptionist — G. Haufschild

ST. BONIFACE UNIT

Supervisor — E. Oleski (G. Devisscher, Acting Supervisor 21 June to 31 Dec.)
Cancer Registry Officer — G. Devisscher
Medical Transcriptionists — L. Soshycki, G. Taylor, J. Olson
Records Processing Clerk — K. Friesen
Records Control Clerk — M. Morrison
Receptionist — C. MacLean

As the health information processing centre for the Manitoba Cancer Treatment and Research Foundation, the Records and Registry Department is comprised of the following functional units:

HEALTH RECORDS SERVICES

With a staff complement of 13.5 EFT, this unit's scope of service comprises the following:

- Health Record Filing, Control and Retrieval
- Medical Transcription Services
- Patient Registration, Documentation, and Data Collection
- Intake Co-ordination (New Patient Referral Processing)
- Coordination and Documentation of Diagnostic Reports
- Release and Distribution of Patient Information
- Reception and Switchboard Services
- Courier Services/Mail Processing

In 1988, this unit continued to hone its systems to more effectively provide its broad range of clinical health records services.

New patient statistics show an increase of 12% since 1987. This, along with the longer term and increasingly complex nature of cancer treatment, has caused Health Records Services workloads to rise considerably. The re-organization and development efforts of the past number of years bore fruit in 1988, when, despite consistently increasing workloads, quantitative and qualitative elements of performance began to stabilize at acceptable levels. This will provide the basis for expansion and enhancement of services into those areas targeted for some time, namely: care quality audit, quantitative analysis of clinical documentation, and facility utilization evaluation. Such enhancement would in turn contribute to the efforts towards accreditation of the Foundation in the future.

In the latter part of 1988, funding was approved for the acquisition of a new dictation/transcription system. As a result, the next year will see the installation of a state-of-the-art centralized system, utilizing digital technology. It is anticipated that the new system will provide significant benefit to clinical users and department systems.

The Unit continued to support the Foundation's Outreach Program, which through its consistent growth has become a significant user of the department's services.

The new Health Record Liaison Committee provided a valuable forum for resolution of multidisciplinary issues, co-operative development of new systems and introduction of record-related policies.

The new Forms Committee commenced its evaluation of the format of the clinical record, with improvement to existing forms, and introduction of several documents which will more effectively facilitate the clinical process.

CENTRAL CANCER REGISTRY

With the staff complement of 10 EFT, the unit's main activities fall within two major areas:

1. The provision of an accurate cancer incidence database for health care planning and quality assurance.
2. The provision of a research database for the detailed study of malignant disease (including epidemiological study, health care delivery analyses, and natural history studies).

The Foundation has been legally mandated to collect, register and maintain data on all cancer cases in Manitoba since 1937. Because of this, data is received from a wide array of primary sources including pathology/cytology reports, admission/separation data from the hospital abstracting system of the Manitoba Health Services Commission, death registration data from the Department of Vital Statistics, and clinical data from individual physicians' offices. This completeness of reporting, along with amalgamation of cancer registry records with treatment records for those patients receiving care at the Foundation, has produced a comprehensive database, which in the last number of years has seen an incremental increase in the number of requests. The nature of requests ranges from simple incidence figures to detailed audit of records based on multiple criteria. Utilization of the expertise residing in our Health Records Technician staff has increased as researchers have become familiar with this resource. The Foundation's Epidemiology and Biostatistics Department remains one of our prime users.

The incidence rates published under separate cover in this Annual Report are based on data collected and compiled by the Central Cancer Registry.

The Central Cancer Registry continues to be an active contributor to the National Cancer Incidence Reporting System and a participating member in the National Cancer Registry Association. In 1988, efforts continued towards the formation of the Canadian Council of Cancer Registries, which will develop and maintain the Canadian Cancer Registry. The Council's mandate will also include ensuring data comparability nationally, developing quality control mechanisms, providing interprovincial death clearance and initiating interprovincial epidemiological studies.

Due to the installation of new radiotherapy equipment, the Central Cancer Registry has been relocated outside the department on a temporary basis. In addition, an inactive records storage area was constructed off-site, but in close proximity to the Foundation. A project was undertaken to identify and wean inactive records from the main health records storage area, thus providing additional active records storage space on a short term basis.

Quality assurance continued to receive significant emphasis in the activities of the Registry in 1988. A unique workload measurement system was developed, tested and implemented, using weighted values for all Registry functions. Qualitative aspects were addressed in regular coding review sessions. A valuable byproduct of these reviews was the development of a comprehensive coding reference manual, which, as well as being utilized within our Registry, provides a central cancer coding resource to health record practitioners throughout the province.

ST. BONIFACE RECORDS AND REGISTRY UNIT

Our satellite Health Records and Registry Unit provides services to our St. Boniface Oncology Department in the same functional areas as the Units located at the main MCF facility. The staff complement consists of 8 EFT. The Unit's progress through 1988 was consistent with that described earlier in the other Units of the Department.

On a department-wide basis, 1988 saw the stabilization of systems and services after a number of years of re-organization and development. It is anticipated that the next major growth spurt in terms of scope of service will occur with the enhancement of computer systems; the development and implementation of a comprehensive computerized health information management system has emerged as the primary thrust of our activities for the future.

INFORMATION SERVICES

Director	H. Schipper, BS Sc MD, FRCP(C)
Assistant Director	P. West

Records and Registry Database Support:

Programmer/Analyst (to April 1988)	J. Ediger
Computer Operator/Data Entry	D. Zimmer

Outreach Cancer Patient Management System
(A conjoint computing project of the MCTRF and the Intelligent Systems Group, the University of Manitoba (U of M)):

Project Advisor (U of M)	D. Scuse, PhD
Programming Staff (U of M)	K. Hotz, MSc J. Anderson, MSc R. McRae, MSc
Knowledge Engineer (MCTRF)	L. Strachan, MSc
Analyst/Domain Coordinator (MCTRF)	B. Burgess, BC Sc

INTRODUCTION

Activities of the Information Services department can be divided into three major categories: support and maintenance of the Records and Registry health information databases, reporting of cancer incidence and mortality statistics (published separately) and technical management of the Outreach Cancer Patient Management System computer project. These activities are discussed in more detail below.

Records and Registry Databases

In 1982, the Medical Information Management System (MIMS) was developed on the newly installed Prime minicomputer. MIMS provides two important online functions: patient registration and tumor registration.

The Patient Registration database (203,850 entries) contains basic demographic information for all patients treated at the MCTRF since 1937. Data recorded includes a central registration number (as well as other hospital and provincial medical registration identifiers), patient name (maiden name and/or known alias where applicable), date of birth (and death), and Foundation physician.

The Tumor Registration database (148,061 entries) contains information about each primary neoplasm that has been reported to the MCTRF since 1937. This includes data with regard to disease site (international disease code, topography, morphology, metastatic sites, and staging information); diagnostic process (date, method, institution); laboratory results; treatment specifics; and where applicable, information related to the death of the patient (date, cause, autopsy results, and Vital Statistics death registration number).

The MIMS has an extensive set of data handling features that allow health record professionals to access patient information with elaborate alphabetic and numeric inquiry procedures, create new records, update the contents of existing records, edit audit-identified discrepancies in records and delete records identified to be duplicate entries.

Cancer Incidence and Mortality Reporting

For additional information, please refer to the Records and Registry section of this report.

Outreach Cancer Patient Management System

Medical computing has traditionally used a data-driven approach in which the computer system is used to maintain patient information that often includes basic demographics, medical history and progress notes, prescribed drugs, treatment schedules, diagnostic data, treatment outcome and other data that is relevant to the management of a patient.

In order to develop computer systems that are more powerful and more flexible than conventional record-keeping systems, researchers continue to investigate the feasibility of developing "intelligent" computers. Artificial intelligence (AI) researchers are developing computer systems that can emulate human cognitive processes like reasoning and learning. Recently, expert systems have received considerable attention in the AI and medical communities. An expert system solves problems in a narrow domain by searching its store of knowledge about that domain. The range of problems that the expert system can solve can be extended by increasing the amount of knowledge that is available.

The Outreach Cancer Patient Management System computing project was formally initiated in 1986. Recruitment and intensive medical orientation was followed by a detailed analysis of the structure of cancer treatment plans and the associated MCTRF clinical support functions.

Since 1987, the Outreach computing team has focussed its attention on the development of a proof-of-concept expert system prototype that facilitates three major functions. First, the prototype supports the interactive definition of treatment regimens, including chemotherapy drugs, diagnostic tests, adverse reaction management criteria and related schedules for predefined treatment plans. Second, the prototype allows patients to be assigned to specific groups within treatment plans. Finally, the prototype assists the healthcare professional in the clinic with the: scheduling of diagnostic test; assessment of diagnostic test results, tracking of toxicity indicators and when necessary, suggesting treatment modifications and follow-up procedures; determination of drug dosage and administration requirements; presentation of clinical data in the form of an active-treatment flowsheet and an archival health record.

User Interface is an area of computing that is concerned with how the user and computer exchange information. It is one of the most important parts of a computer system and when implemented properly, contributes significantly to user acceptance of a system. A significant portion of 1988 was dedicated to conducting a comprehensive review of the user interface literature and the application of this knowledge to the user interface of the prototype.

MANITOBA INSTITUTE OF CELL BIOLOGY

DIRECTOR — A. H. Greenberg, M.D., Ph.D.

FULL TIME SENIOR STAFF:

A. Begleiter, Ph.D.
L. J. Brandes, B.Sc., M.D., F.R.C.P.(C)
D. Chow, Ph.D.
J. M. Gerrard, M.D., Ph.D.
G. J. Goldenberg, M.D., Ph.D., F.R.C.P.(C), F.A.C.P.
S. J. Israels, M.D., F.R.C.P.(C)
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H-Y. P. Lam, Ph.D.
S-T. Lee, Ph.D.
M. Mowat, Ph.D.
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B. A. Schacter, B.Sc.(Med.), M.D., F.R.C.P.(C)
J. A. Wright, B.Sc., M.Sc., Ph.D.

ASSOCIATE MEMBERS:

J. Dodd, Ph.D.
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E. D. Israels, B.A., M.Sc., M.D.

POSTDOCTORAL FELLOWS

J. Batra, R. Brown, A. Deffie, M-C. Gingras, N. Khalil, G. McClarty, A. McNicol, S. Saxena, L. Schwarz, L. Shi, M. Spearman.

GRADUATE STUDENTS

E. Atkinson, S. Battistuzzi, M. Cawker, B. Choy, J. Damen, S. Egan, L. Janz, M. Jesson, J. Hickerson, G. Hicks, S. Hrushovetz, R. Hurta, R. Kraut, T. Osachuk, M. Reese, E. Roussell, P. Sandstrom, C. Seneviratne, A. Tagger, D. Tough, S. Uniyal, W. Yang.

VISITING PROFESSORS (Seminar Series):

Dr. Michael Cole, Dr. Joseph G. Corey, Dr. Dylan Edwards, Dr. Mony Frojmovic, Dr. Michael Gilman, Dr. Tina Haliotis, Dr. David Henner, Dr. Ivan J. Sadowski, Dr. B. N.Y. Setty, Dr. James White.

VISITING PROFESSORS (Research):

Dr. L. Hoffman-Goetz, Dr. B. N. Y. Setty, Dr. E. Turley.

VISITING SCHOLARS:

X. Lu, J. Q. Lu, L. Lin.

SUMMER STUDENTS

B. Ballon, J. Carter, T. Kolodka, M. Pimental, B. Tiwari.

TECHNICIANS

C. Anhalt, O. Bereznay, P. Bogdanovic, A. C. Chan, A. Chan, M. Chapiel, V. Cripps, M. Daniels, L. M. Desilets, K. Devine, J. Dickson, E. Duta, W. Finnigan, L. Heinemann, L. Jarolim, D. Johnson, H. Joling, K. Kamali, M. Leith, A. Levy-Hall, D. Lint, L. Lin, A. Low, J. Maeba, E. McMillan, S. Oh, S. Ozomoto, A. Polonyi, C. Robertson, P. Robinson, E. Robotham, M. Sauder, R. Singal, S. Singhroy, B. Sukhu, N. Swiridenko, C. Switzer, M. Talgoy, K. Tang, E. Taylor, C. Ulicki, T. Van Denakker, L. Verburg, M. Wilcock.

LAB ASSISTANTS

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SECRETARIES

G. Morgan, S. Richter, S. Schiissler, S. Snusher, A. Warkentin.

THE MANITOBA INSTITUTE OF CELL BIOLOGY

The Manitoba Institute of Cell Biology was founded jointly by the University of Manitoba and the Manitoba Cancer Treatment and Research Foundation in 1969. The purpose of the Institute is to carry out research and training in cancer and other diseases by studying disease mechanisms at a cellular and molecular level. The Institute of Cell Biology is governed by an independent Board of Management consisting of eleven members, three appointed by the University of Manitoba, three appointed by the Manitoba Cancer Treatment and Research Foundation and five jointly appointed by both sponsoring Institutions. The Manitoba Institute of Cell Biology is housed in the Manitoba Cancer Treatment and Research Foundation adjacent to the Faculty of Medicine, University of Manitoba and the Health Sciences Centre.

The Institute of Cell Biology consists of a Director, thirteen senior investigators, and ninety staff including research associates, postdoctoral fellows, graduate students, technicians, laboratory assistants and secretaries. Although the Institute of Cell Biology is not a degree-granting body, advanced degrees at the Masters or Ph.D. level may be obtained with any of the departments in the Faculty of Medicine, University of Manitoba. The major emphasis of the research program of the Institute of Cell Biology has centered on the fields of Molecular Biology of Tumor Progression, Biochemical Pharmacology, Drug Resistance, Immunology and Hematology. Senior investigators hold cross-appointments in many University departments including the Departments of Immunology, Genetics, Biochemistry, Physiology, Microbiology, Medicine and Pediatrics.

The location of the Manitoba Institute of Cell Biology in the Manitoba Cancer Treatment and Research Foundation building has enabled the development of parallel programs of basic and clinical investigation of patients with neoplastic disease. Patients with a wide range of neoplastic disorders are available for investigation conducted by senior investigators in the Institute. Not only is this interaction facilitated by a geographical juxtaposition of the two Institutions, but also by the fact that many senior investigators hold cross-appointments in the Manitoba Institute of Cell Biology and Manitoba Cancer Treatment and Research Foundation.

The Manitoba Institute of Cell Biology is only one of the two Institutes in Canada funded by the National Cancer Institute, and has been continually supported by the NCI since the inception of the Institute group in 1969. During the 1988-89 academic year, members of the Institute received $2.7 million dollars in research funds, of which $0.7 million was for career awards, postdoctoral fellowships and studentships. Funding sources include the NCIC, MRC, NSERC, NIH, many smaller foundations, as well as private industry (Bristol-Myers, Park Davis, RJ Reynolds). This represents about 15% of the total research funds won by the Faculty of Medicine and one of the highest per capita funding rates of all Departments. In the last year a change in the source of research funding has become evident with a significant portion of our operating grants now coming from industry, in particular pharmaceutical houses, as well as the National Institutes of Health in the United States.

It is with pleasure that the Institute announces that three staff members now hold career awards including Dr. Jim Wright (National Cancer Institute Research Associate), Dr. Jon Gerrard (Medical Research Council Scholar) and Dr. Arnold Greenberg (Terry Fox Research Scientist). In addition, in this last year six postdoctoral fellowships were won in national and provincial competitions; Dr. Maureen Spearman (MRC), Dr. N. Khalil (Parker Francis Foundation), Dr. A. McNicol (MHRC), Dr. S. Saxena (MCF), Dr. M.-C. Gingras (MHRC) and Dr. G. McClarty (U. of Manitoba); and eleven graduate students won competitive studentships; S. Egan (NCI, Steve Fonyo), J. Broere (NSERC), E. Atkinson (MHRC), S. Unival (MHRC), S. Battistuzzi (MRC), T. Osachuk (MRC), J. Damen (NSERC), L. Janz (NSERC), R. Choy (MHRC), P. Sandstrom (MCF), W. Yang (MCF).

During 1988, we were fortunate to have visiting scientists at the Institute either lecturing, taking part in collaborative studies or spending their sabbatical research leave with members of the Institute:

Visiting Professors (Seminar Series):

Dr. Joseph G. Cory, University of South Florida, Tampa, Florida.
"Unique Aspects of Ribonucleotide Reductase as a Chemotherapeutic Target"

Dr. David Henner, Dana-Farber Cancer Institute, Boston, Mass.
"Glutathione Transferases and Anticancer Drug Resistance"

Dr. A. Petkau, Atomic Energy of Canada, Pinawa, Manitoba.
"Protection of Bone Marrow Progenitor Cells by Superoxide Dismutase"

Dr. J. Kanfer, University of Manitoba, Dept. of Biochemistry
"Glycerolphosphorylcholine Diesterases of Brain Tissues"

Dr. Michael Cole, Princeton University, Princeton, N.J.
"The c-*myc* Oncogene and Cell Transformation"

Dr. Mony Frojmovic, McGill University, Montreal, P.Q.
"Cellular Membrane Rearrangements Associated with Platelet Aggregation Studies Using Microscopy and Particle Counting"

Dr. Dylan Edwards, Oxford University, Oxford, England.
"Growth Factor Regulated Genes"

Dr. Tina Haliotis, Mount Sinai Hospital Research Institute, Toronto, Ont.
"Biochemical aspects of *ras*-induced transformation"

Dr. James White, University of Minnesota
"Platelet Shape Change: The Membrane That Moves"

Dr. Michael Gilman, Cold Spring Harbor Laboratory, N.Y.
"Intracellular Mediators of c-*fos* by Extracellular Signals

Dr. Ivan J. Sadowski, Harvard University, Boston, Mass.
"New Approaches to the Analysis of Transcriptional Activators"

Dr. B. N. Y. Setty, Temple University, Philadelphia, PA.
"Effect of Hydroxy-Eicosanoids on Endothelial Cell Functions"

Dr. J. Davie, University of Manitoba, Dept. of Biochemistry
"Characterization of Trout Hepatocellular Carcinonomas Induced by Aflatoxin B_1"

Dr. R. Matusik, University of Manitoba, Dept. of Physiology
"Identification of M-40 as a New Ligand Carrier Family"

Dr. J. Geiger, University of Manitoba, Dept. of Pharmacology and Therapeutics
"Adenosine Transport in the Central Nervous System"

Dr. F. Jay, University of Manitoba, Dept. of Medical Micro.
"High Level Expression of Human Interferon-Gamma in Bacteria"

Visiting Professors (Research):

Dr. E. A. Turley, University of Alberta, Calgary, Alta.
Phosphoinositide catabolism with Dr. J. Gerrard and Hyalurate on H-*ras* transformation with Dr. A. H. Greenberg.

Dr. L. Hoffman-Goetz, Unviersity of Waterloo, Ontario
(Sabbatical leave) Brain-immune interactions with Dr. A. H. Greenberg.

Dr. B. N. Y. Setty, Temple University, Philadelphia, PA.
Hydroxy-eicosanoids with Dr. J. Gerrard.

A. MOLECULAR BIOLOGY/TUMOR PROGRESSION

MOLECULAR MECHANISMS OF DRUG RESISTANCE INVOLVING RIBONUCLEOTIDE REDUCTASE; HYDROXYUREA RESISTANCE IN A SERIES OF CLONALLY RELATED MOUSE CELL LINES SELECTED IN THE PRESENCE OF INCREASING DRUG CONCENTRATIONS

Bob K. Choy, Grant A. McClarty, Arthur K. Chan, Lars Thelander, and Jim A. Wright.

Mammalian ribonucleotide reductase is a highly regulated, rate-limiting activity responsible for converting ribonucleotide diphosphates to the deoxyribunucleotide precursors of DNA. The enzyme consists of two nonidentical proteins often called M1 and M2, both of which are required for activity. Hydroxyurea is an antitumor agent which inhibits ribonucleotide reductase by interacting with the M2 component specifically at a unique tyrosyl free radical. To obtain further information about drug resistance mechanisms, we have used M1 and M2 complementary DNAs and monoclonal antibodies to investigate the properties of a series of clonally related drug-resistant mouse cell lines, selected by a step-wise procedure for increasing levels of resistance to the cytotoxic effects of hydroxyurea. Several interesting mechanisms have been identified. Each successive drug selection step leading to the isolation of highly resistant cells was accompanied by stable elevations in cellular resistance and ribonucleotide reductase activities. The changes that occurred at each step involved the M2 component. A very early event, occurring at the first step in the selection process, was the amplification of the M2 gene accompanied by an increase in M2 messenger RNA. Although cellular resistance and M2 protein levels increased significantly during drug selection, only a modest change in M2 gene copy number was observed after the initial selection step. Analysis of wild type, moderately resistant, and highly resistant cells indicated that, in addition to M2 gene amplification, posttranscriptional modification also occurred during drug selection. This second mechanism was not due to alterations in protein M2 half-life, but involved an increase in translational efficiency. By increasing the rate of M2 synthesis, without altering degradation rates, resistant cells were able to accumulate high levels of this key regulatory protein. Cells selected for the ability to proliferate in concentrations of drug as high as 4mM exhibited changes that involved M2, without detectable changes to M1. These results provide further evidence that M1 and M2 levels are controlled by different mechanisms in mammalian cells. Eventually, however, cells required an elevation in the M1 protein, as well as the M2 protein, to survive in a hydroxyurea concentration of 5mM. These results illustrate the complexity of the drug-resistant phenotype and provide further information about the molecular processes that lead to the development of cells resistant to low, intermediate, and high concentrations of hydroxyurea.

EXPRESSION OF GROWTH FACTORS AND GROWTH FACTOR RECEPTORS IN HUMAN PROSTATIC DISEASE

Janice G. Dodd, Gary Morris, Zhi Qin

Our understanding of the function of the prostate gland at the molecular level and of the onset of disease in this gland is very limited. Steroid hormones and peptide growth factors are known to influence the growth and secretory role of the prostate, but the mechanisms remain unknown. Our objective is to apply the tools of molecular biology to the study of several genes which may be involved in the regulation of prostatic growth and function. two of these genes code for related peptide growth factors, epidermal growth factor (EGF) and transforming growth factor-alpha (TGF-α). A third gene codes for the cell membrane receptor for EGF and TGF-α. Together these gene products represent a potential growth control pathway. Alterations in the expression of one or more of these genes may lead to altered control of prostate growth. We have recently demonstrated that one of these gene products, the EGF receptor, is expressed at a higher level in prostatic carcinomas than in non-malignant prostatic tissue. We are currently examining the expression of the other genes of the pathway in order to determine their correlation with the occurrence of prostate disease. Using prostatic cell culture systems, we are studying the regulation of expression of the genes in this growth control pathway.

HUMAN PAPILLOMAVIRUS INFECTION AND PROSTATE NEOPLASIA

Janice G. Dodd and Patricia J. McNicol (Cadham Provincial Laboratories)

The objective of this study is to examine the involvement of human papillomavirus in prostatic diseases. Although a viral etiology for prostatic cancer has been suggested in the past, standard virological techniques have failed to resolve the question. The growing body of literature implicating a variety of human virtues in human cancers and, in particlar, the compelling evidence linking certain sexually transmitted HPV types with uterine cancer in women, led us to re-examine the question of viral involvement in human prostatic disease. The recent availability of molecular probes for several HPV types have made this study possible. We have demonstrated by Southern analysis, the presence of HPV-related sequences in both benign hyperplasia and carcinomas of the prostate. We are currently continuing our analysis of HPV sequences in human prostate tumors using the polymerase chain reaction (PCR) procedure, a highly specific and sensitive assay. We are assessing the frequency of HPV infection of prostate neoplasias and the specific types of HPV involved. Molecular characterization of the viral sequences in these tumors will include cloning, DNA sequencing, mapping and assaying of expression of both viral genes and cellular oncogenes. From these studies we will be able to determine the potential role of the HPV virus in the development of prostate tumors.

H-ras EXPRESSION AND METASTASIS FORMATION

Sean E. Egan, Grant A. McClarty, Lenka Jarolim, Jim A. Wright, Ira Spiro, Gordon Hager, and Arnold H. Greenberg

Using three independent approaches, we have studied the effects of H-ras on metastasis formation. Transformation of two nonsenescing murine fibroblasts 10T½ and NIH-3T3, by H-ras oncogenes consistently produced metastatic tumor lines. Analysis of five in vitro ras-transfected 10T½ clones revealed a relationship between metastatic potential and H-ras expression. Four metastatic variants derived from a poorly metastatic, low H-ras expressing line all express high levels of H-ras RNA. Activation of H-ras expression in the metastatic tumors had occurred through amplification and rearrangement of H-ras sequences. In addition, preinduction of p21 synthesis in NIH-3T3 line 433, which contained v-H-ras under the transcriptional control of the glucocorticoid-sensitive mouse mammary tumor virus long terminal repeat (MMTV LTR), significantly increased metastatic efficiency. This study demonstrates a correlation between metastatic potential and H-ras expression, suggesting that progression to the matastatic phenotype may occur through selection of variants with enhanced oncogene expression.

SELECTION OF VARIANTS WITH ALTERED EXPRESSION OF EXTRACELLULAR MATRIX AND PROTEASE GENES DURING LUNG IMPLANTATION OF METASTATIC H-*ras* TRANSFORMED FIBROBLASTS

M. C. Gingras, L. Jarolim, J. A. Wright, and A. H. Greenberg

To elucidate the processes that contribute to in vivo metastatic progression, 10T½ fibroblasts transformed by a plasmid containing H-ras and neo were injected into C3H mice, and recovered from lungs by enzymatic treatment and selective outgrowth of G418. Less than 1 in 10^3 cells survived in the lung 30 min after inoculation and these exhibited a unique phenotype. This was characterized by a propensity to lodge in the lung on reinjection, a markedly enhanced expression of collagen and fibronectin, and decreased expression of laminin, cathepsin L, transin and H-*ras*, a phenotype which was similar to the untransformed parental fibroblast. No change in c-*myc*, GAP or β-actin expression was observed. Despite their much improved ability to remain in the lung, these cells were only slightly more metastatic than the injected tumor. Following a further 95% reduction in viable tumor in the lung over the next 24 hours, the tumor cells were proliferated rapidly. Between 1 and 9 days after injection, the cells reacquired the original pattern of gene expression of the injected tumor, but were now 26-fold more metastatic. We hypothesize that two selection events have occurred; the first, for lung homing and implantation, occurs in variants with high matric and low protease expression. and, the second, for cells that carry a favorable phenotype for invasion and proliferation. The similarity between these latter cells and the injected line indicates that selection for properties other than those already studied are responsible for their enhanced metastatic ability.

IN VIVO METASTATIC PROGRESSION OF AN H-ras TRANSFORMED MOUSE 10T½ CELL LINE

M.-C. Gingras, L. Jarolim, J. A. Wright, and A. H. Greenberg

Experiments from this laboratory have demonstrated that the metastatic efficiency of a series of H-ras transfected fibroblasts correlates with the expression of the oncogene. We now tested the hypothesis that the ability of a ras-transformed line to survive in the lung may be related to ras expression. If this were the case, then preferential selection of high H-ras-expressing, increasingly metastatic variants may be observed during early lung growth. A T-24-H-ras transformed mouse 10T½ fibroblast clone was injected i.v. into C3H/HeN mice and tumor cells were recovered from the lungs at different times (30 min, 1, 9 and 21 days) from the lungs by selective growth in G418 sulfate. Their metastatic efficiency was tested in vivo and ras expression evaluated by Northern blotting. We report that lung-derived tumor cells show a gradual increase in their metastatic ability over the first 9 days of implantation, and that this is an unstable characteristic which is lost with prolonged growth in vivo or in vitro. No increase in the transcriptional activity of the ras gene was detected in variants with a 27-fold increase in metastatic ability. We conclude that while the metastatic efficiency of in vitro transformed lines is dependent on the expression of the ras gene, metastatic progression in vivo can be independent of ras transcription. It was previously reported by this laboratory that natural killer (NK) cells can control the number of metastatic cells surviving in the lung. The same experimental protocol was repeated in natural-killer-cell-deficient bg/bg mice. A similar pattern of metastatic potential of tumor cells recovered from bg/bg mice and normal bg/+ mice was observed, which permits us to exclude the possibility that the selection process was the result of increased survival of NK cell-resistant variants.

INTEGRATION OF FRIEND MURINE LEUKEMIA VIRUS INTO BOTH ALLELES OF THE P53 ONCOGENE IN AN ERYTHROLEUKEMIC CELL LINE

Geoffrey G. Hicks and Michael Mowat

We have described several Friend virus induced erythroleukemia cell lines that have undergone rearrangement of the p53 oncogene. These rearrangements result in complete inactivation of the p53 gene or production of truncated forms of p53 protein. Further, altered cell lines occur in nearly 50% of the mice. The Friend Virus transformed erythroleukemic cell line DP16-2 has undergone a complex rearrangement of the p53 oncogene and lacks any detectable expression of the p53 gene product. We report here characterization of both p53 alleles in this cell line and identify independent integrations of F-MuLV sequences into the coding region of both alleles. Restriction map analysis of molecular clones for both rearranged alleles reveal the insertion of a 2.3Kb or 3.5Kb DNA sequence into the coding region of p53. These inserts show specific hybridization to FMuLV probes and have restriction map homology with the FmuLV provirus. Both integrations were followed by a deletion of most of the viral sequences and a region of exon 10 of one allele, and a region of exons 5 to 7 of the other allele. Helper virus inactivation of p53 is therefore likely an important step in the progression of this leukemia.

ALTERED RESPONSIVENESS OF METASTATIC VERSUS NON- METASTATIC FIBROBLASTS TO HEPARIN-BINDING GROWTH FACTORS

L. C. Schwarz, J. E. Damen, A. H. Greenberg and J. A. Wright

Cells may become more metastatic partially by gaining growth factor autonomy. This hypothesis was examined by investigating the effects on DNA synthesis of a novel hepatic heparin-binding growth factor (HBGF), and of the well-characterized HBGF, basic fibroblast growth factor (bFGF), using cells of varying metastatic potential. Cells were rendered metastatic by transfection of parental 10T½ fibroblasts with the T24-H-ras oncogene. Both HBGFs stimulated DNA synthesis 2.0-11.1 fold in 10T½ cells in the presence of ∝-minimal essential medium containing 10% fetal bovine serum. In contrast, cells of intermediate metastatic potential or of high metastatic potential, were inhibited approximately 2-fold by the hepatic HBGF, and did not respond to bFGF in ∝-minimal essential medium plus 10% fetal bovine serum. This lack of stimulation was converted to an enhancement of DNA synthesis in the absence of serum when using metastatic but not non-metastatic cells. This is the first demonstration that metastatic cells have a significantly altered responsiveness to these growth factors as compared to non-metastatic parental cells, and indicates that these modifications may play a role in a mechanism of tumor progression.

MOLECULAR MECHANISMS RESPONSIBLE FOR THE DRUG-INDUCED POSTTRANSCRIPTIONAL MODULATION OF RIBONUCLEOTIDE REDUCTASE LEVELS IN A HYDROXYUREA-RESISTANT MOUSE L CELL LINE

Grant A. McClarty, Arthur K. Chan, Bob K. Choy, Lars thelander and Jim A. Wright

Ribonucleotide reductase, which catalyzes the formation of deoxyribonucleotides from ribonucleoside diphosphate precursors, is the rate-limiting enzyme in DNA synthesis. The enzyme consists of two nonidentical subunits called M1 and M2, both of which are required for activity. Hydroxyurea, a specific inhibitor of DNA synthesis, acts by destroying the unique tyrosyl free radical of protein M2. Previously, we have described a mouse L cell line which exhibited a stable resistance to high concentrations of hydroxyurea. This mutant cell line contains elevated quantities of both proteins M1 and M2 as a result of corresponding increases in the levels of nRNAs for both subunits. Interestingly, both M1 in the presence of hydroxyurea, and this elevation was not accompanied by increases in their corresponding mRNAs. These results indicated that hydroxyurea can modulate ribonucleotide reductase expression posttranscriptionally. In this report, we show that the level of both subunits of ribonucleotide reducatase responds to hydroxyurea in a drug concentration dependent manner. Furthermore, results from kinetic studies indicate that protein M2 levels rise much more rapidly than protein M1. Pulse-chase experiments indicated that the half-lives of both the M1 and M2 polypeptides are increased by approximtely 2-fold when the mutant cells are cultured in the presence of hydroxyurea. We also present evidence indicating that exposure of these cells to hydroxyurea leads to a relatively slow but specific increase in the rate of biosynthesis of both proteins M1 and M2, as assayed by pulse labeling. Therefore, we conclude that both components of ribonucleotide reductase are synthesized at an increased rate and turn over at a slower rate when these mutant cells are grown in the presence of hydroxyurea. In addition, experiments were performed to examine the effects of exogenously added iron on the biosynthesis of proteins M1 and M2. Interestingly, the results suggested a role for iron in regulating the level of M2 protein when cells are cultured in hydroxyurea-supplemented medium.

RELATIONSHIPS BETWEEN REVERSION OF HYDROXYUREA RESISTANCE IN HAMSTER CELLS AND CO-AMPLIFICATION OF RIBONUCLEOTIDE REDUCTASE M2 COMPONENT, ORNITHINE DECARBOXYLASE AND P5-8 GENES

G. A. McClarty, P. N. Tonin, P. R. Srinivasan and J. A. Wright

Hydroxyurea is a specific inhibitor of ribonucleotide reducatase, which is a rate-limiting enzyme activity in DNA synthesis. Cells selected for resistance to hydroxyurea contain alterations in ribonucleotide reducatase activity. An unstable hydroxyurea resistant population of hamster cells has been used to isolate a stable drug resistant cell line, and two stable revertant lines with different sensitivities to hydroxyurea cytotoxicity and different ribonucleotide reducatase activity levels. We show for the first time that a decrease in hydroxyurea resistance is accompanied by a parallel decline in gene copies for the M2 component of ribonucleotide reducatase, ornithine decarboxylase and a gene of unknown function called p5-8, indicating that the co-amplification of the three genes is associated with drug resistance, and supporting the concept that M2, ornithine decarboxylase and p5-8 are closely linked, and form part of a single amplicon in hamster cells.

LOSS OF GROWTH FACTOR DEPENDENCE AND CONVERSION OF TRANSFORMING GROWTH FACTOR-β_1 INHIBITION TO STIMULATION IN METASTATIC H-ras-TRANSFORMED MURINE FIBROBLASTS

Lois C. Schwartz, Marie-Claude Gingras, Grant Goldberg, Arnold H. Greenberg and Jim A. Wright

Cell lines with varying tumorigenic and metastatic potentials have been obtained by transformation of 10T½ fibroflasts using radiation or transfection with T-24 H-ras. We have observed an inverse relationship between metastatic potential and dependence on serum for growth. The effects of basic fibroblast growth factor, platelet-derived growth factor, epidermal growth factor, and transforming growth factor-β_1 (TGF-β_1) on these lines were then examined to determine if the changes in the serum dependence of metastatic cells may be due to altered responsiveness to specific growth factors (GFs). Cells were grown in monolayer culture and DNA synthesis was measured by [CH_3-^{3}H]thymidine incorporation experiments. Both metastatic and nonmetastatic cells were shown to be equivalent in their diminished responsiveness to basic fibroblast growth factor, platelet-derived growth factor, and epidermal growth factor as compared to their nontransformed, parental 10T½ cells. However, a unique response of metastatic cells to TGF-β_1 was identified. While TGF-$\beta_1$inhibited DNA synthesis in 10T½ cells and a nonmetastatic tumor, cells with intermediate to high metastatic ability were stimulated up to 5.8-fold by TGF-β^1. Interestingly, epidermal growth factor abrogated the TGF-β_1 inhibition of the parental 10T½ cells, but had no effect on the TGF-β_1 response of any metastatic line. Therefore, metastatic but not nonmetastatic cells, demonstrated a dramatically altered sensitivity to TGF-β_1, a response which may be important in determining metastatic potential.

MOLECULAR AND CELLULAR CHARACTERIZATION OF DRUG RESISTANT HAMSTER CELL LINES WITH ALTERATIONS IN RIBONUCLEOTIDE REDUCTASE

Aaron Y. Tagger and Jim A. Wright

Ribonucleotide reductase consists of 2 protein components frequently called M1 and M2. Hydroxyurea specifically inhibits DNA synthesis by interacting with the M2 protein and destroying a unique tyrosyl-free radical. We have carried out a molecular and cellular characterization of 2 Chinese hamster ovary cell lines exhibiting either low (HN^R-AT) or relatively high (H^R-R2T) resistance to cytotoxic effects of hydroxyurea. Both drug-resistant lines have an increased level of ribonucleotide reductase activity. EPR measurements for tyrosyl-free radical content and studies with M1-specific antibodies indicated that the elevation in enzyme activity was entirely due to an increase in the M2 component. Studies with M1 cDNA showed that both drug-resistant cell lines contained a wild-type level of M1 mRNA and a wild-type M1 gene copy number. Studies with M2 cDNA indicated that the 2 drug-resistant lines possessed elevated levels of M2 message that could explain the observed increase in M2 component. The elevation of M2 mRNA in the most resistant line, H^R-R2T, was due to an increase in M2 gene copy number. The low resistant cell line, HN^R-AT, exhibited a wild-type M2 gene copy number, indicating that the increase in M2 gene message occurred through a process other than gene amplification. Enzyme kinetic studies with partially purified preparations from both drug resistant lines showed reduced sensitivity to hydroxyurea and to the negative allosteric effector, dATP. In addition to hydroxyurea, H^R-R2T cells were also resistant to several other drugs whose site of action is the M2 component. Furthermore, H^R-R2T cells were not cross-resistant to colchicine or puromycin, suggesting that hydroxyurea-resistant cells do not share the multi-drug resistance phenotype, which is frequently associated with cross-resistance to these drugs.

STRUCTURALLY DIVERGENT ONCOGENES INDUCE THE METASTATIC PHENOTYPE

S. E. Egan, J. A. Wright, L. Jarolim, K. Yanagihara, R. H. Bassin, A. H. Greenberg

We and others have established that the *ras* oncogene can transform established rodent fibroblast cell lines into fully metastatic tumors and that the metastatic behavior of these cells is directly regulated by *ras*. In subsequent work, we found that overexpression of *ras* as well as mutations effecting GTPase, nucleotide binding or exchange, all transform NIH-3T3 to metastatic tumors. These results support a role for increased ras-GTP active complex in regulating metastatic behavior of *ras* transformed cells. It is clear, however, that not all human tumors contained activated or greatly overexpressed *ras* genes. To directly test the hypothesis that other oncogenes may be involved in regulating or inducing the metastatic phenotype we have assessed the ability of NIH-3T3 (clone 7) cells transformed by various oncogenes to form metastases. Cell lines transformed by the serine/threonine kinase oncogenes v-*raf*, A-*raf*, or v-*mos* as well as the tyrosine kinase oncogenes v-*src*, v-*fes* or v-*fms* were metastatic. In contrast, cells transformed by either of two nuclear oncogenes, *myc* or p53, were tumorigenic when injected subcutaneously but were virtually non-metastatic. Control NIH-3T3 or NIH-3T3 infected or transfected with MoMuLV were also non-metastatic. These data demonstrate that, in addition to *ras*, a structurally divergent group of kinase oncogenes can induce the metastatic phenotype.

A. BIOCHEMICAL PHARMACOLOGY/DRUG RESISTANCE

INCREASED SENSITIVITY OF QUINONE RESISTANT CELLS TO MITOMYCIN C

Asher Begleiter, Erica Robotham, Glen Lacey, and Marsha K. Leith

L5178Y cells resistant to the model quinone antitumor agent, hydrolyzed benzoquinone mustard, were 4-fold more sensitive to mitomycin C compared to parental cells. Mitomycin C also produced increased DNA-DNA crosslinking in these cells compared to parental L5178Y cells, but did not induce DNA double strand breaks in either cell line. The resistant cells have a 24-fold increased level of DDT-diaphorase activity, an enzyme that produces two electron reduction of quinone groups. Dicoumarol, an inhibitor of DT-diaphorase, significantly inhibited crosslinking and cytotoxicity by mitomycin C in the quinone resistant cells. These findings suggest that DNA-DNA crosslinking may be a major contributor to mitomycin C ccytotoxic activity in L5178Y cells, and that the hydroquinone of mitomycin.

CHARACTERIZATION OF L5178Y MURINE LYMPHOBLASTS RESISTANT TO QUINONE ANTITUMOR AGENTS

Asher Begleiter, Marsha K. Leith, Grant McClarty, Samuel Beenken, Gerald J. Goldenberg and Jim Wright

The exact contribution of the quinone group to the activity of quinone antitumor agents remains uncertain. Two L5178Y murine lymphoblastic cell lines resistant to the model quinone antitumor agent, hydrolyzed benzoquinone mustard, and one partial-revertant cell line were isolated and characterized. The antitumor activity of hydrolyzed mustard has been shown previously to be due to its ability to induce free radical mediated DNA strand breaks. Resistant cells were obtained by growing a cloned L5178Y parental cell line in media containing increasing concentrations of hydrolyzed benzoquinone mustard. L5178Y/HBM2 cells were selected from L5178Y cells growing in media containing 0.2 nM drug, while L5178Y/HBM10 cells were selected from cells growing in media containing 1.0 nM drug. The L5178Y/HBMR cells were obtained by growing L5178Y/HBM10 cells in media without hydrolyzed benzoquinone mustard. The resistant cell lines, L5178Y/HBM2 and L5178/HBM10 were 2.5- and 6-fold less sensitive, respectively, to hydrolyzed benzoquinone mustard compared to parental cells, and this was accompanied by a decrease in the formation of DNA single and double breaks by this drug. The partial-revertant cell line, L5178Y/HBMR was 2.9-fold less sensitive to hydrolyzed benzoquinone mustard compared to parental cells.

Drug uptake appeared to be lower in the resistant cells compared to parental cells. The resistant cells had a slightly elevated level of superoxide dismutase activity compared to parental cells, but there was no increase in the mRNA for superoxide dismutase nor any amplification of the gene for this enzyme. Intracellular catalase activities of the L5178Y/HBM2 and L5178Y/HBM10 cells were elevated by 1.25- and 2.6-fold, respectively, and the increased enzyme activity in the L5178Y/HBM10 cells appeared to result from a 3.6-fold increase in mRNA for this enzyme. Glutathione peroxidase activity was slightly elevated in L5178Y/HBM2 cells, but was unchanged in the other resistant cells. The L5178Y/HBM2 and L5178Y/HBM12 cells showed increased concentrations of glutathione and elevated levels of glutathione transferase activity. The resistant cell lines also had DT-diaphorase activity that was 3- and 24-fold higher in L5178Y/HBM2 and L5178Y/HBM10 cells, respectively, compared to sensitive cells. However, cytochrome P-450 reductase activity and the ratio of reduced to oxidized pyridine nucleotides was unchanged in the resistant cell lines.

The parital-revertant cell line, L5178Y/HBMR, showed approximately the same level of resistance to hydrolyzed benzoquinone mustard as the L5178Y/HBM2 cells. This lower degree of resistance compared to L5178Y/HBM10 cells was accompanied by a decrease in glutathione concentration to a level below that found in the parental cells and a decrease in DT-diaphorase activity to the level found in L5178Y/HBM2 cells. The catalase and glutathione transferase activities were only slightly decreased in the revertant cells compared to L5178Y/HBM10 cells.

These studies suggest that resistance to hydrolyzed benzoquinone mustard in L5178Y/HBM2 and L5178Y/HBM10 cells is multifactorial. Drug uptke may be decreased in the resistant cells. Elevated levels of DT-diaphorase may lead to preferential reduction of the hydrolyzed benzoquinone mustard quinone ring directly to the hydroquinone, thus decreasing the formation of the hydrolyzed benzoquinone mustard semiquinone and of oxygen free radicals and hydrogen peroxide. In addition, increased levels of glutathione, glutathione transferase activity, glutathione peroxidase, and catalase activity may also contribute to the resistance in these cells by inactivating free radicals and hydrogen peroxide generated by redox reactions of the quinone agent. These resistant cell lines should prove valuable in evaluating the role of the quinone agent. These resistant cell lines should prove valuable in evaluating the role of the quinone group in the cytotoxic activity of quinone antitumor agents.

GROWTH-PROMOTING ACTIVITY OF DESMOPRESSIN IN MURINE LEUKEMIA CELLS TREATED IN VITRO

Samuel W. Beenken, Janendra K. Batra, Jonathan M. Gerrard and Gerald J. Goldenberg

The synthetic vasopressin analogue, desmopressin (dDAVP), has been shown to influence membrane transport of melphalan in murine L5178Y lymphoblasts. Accordingly, the effect of dDAVP on the cytocidal activity of melphalan in L5178Y cells was evaluated. dDAVP did not affect the cytocidal activity of melphalan in these cells, but significantly affected the cloning efficiency of stationary phase or slowly dividing L5178Y cells over a range of concentrations. In particular, stationary phase cells showed an increase in cloning efficiency from 4.3 ± 0.5% in control cells to 7.0 ± 0.3% in cells treated with 25 nM dDAVP ($P > 0.001$), whereas cells doubling every 26 h showed an increase from 10.8 ± 1.2% in control cells to 21.0 ± 2.0% in cells treated with 150 nM dDAVP ($P < 0.001$). This phenomenon was associated with significant elevations of 1,2[^{3}H] diacylglycerol after incubation with dDAVP for 9 min ($P < 0.01$) and of total [^{3}H] diacylglycerols after incubation for both 3 min ($P < 0.05$) and 9 min ($P < 0.02$). Within 10 s of treatment with 100 nM dDAVP, there was a marked decrease in the levels of inositol 1,4,5-trisphosphate and inositol 1-phosphate, but subsequently no change was observed for up to 9 min after treatment. We postulate that the increase of diacylglycerol content produced by dDAVP might be primarily from a phosphatidylcholine source and that the growth-promoting activity of desmopressin may be a consequence of activation of protein kinase C.

MEMRANE TRANSPORT CHANGES IN AN ADRIAMYCIN-RESISTANT MURINE LEUKEMIA CELL LINE AND IN ITS SENSITIVE PARENTAL CELL LINE

Ratna Bose and Hing-Yat Peter Lam

Multidrug resistance in cancer chemotherapy occurs when cells develop resistance towards structurally and functionally unrelated drugs. It is speculated that alteration of some fundamental process(es) in the cells leads to the development of multidrug resistance. The sodium pump activity of murine leukemia cell lines P388/S (sensitive) and P388/ADR (resistant) was measured and found to be different in the two cell lines. The rate of sodium pumping, i.e. the ouabain-sensitive rubidium uptake, was consistently lower in the resistant cells compared to their parental controls. Uptake of adriamycin was lower in the resistant cells. Depolarizing the cells with potassium chloride or by inhibiting the pump with ouabain increased the adriamycin uptake in the sensitive cells but not in the resistant cells. Adriamycin did not have any acute effects on the sodium pump activity. It is concluded that the development of drug resistance in cell line P388 is associated with a decrease in sodium pump activity and a lack of depolarization-induced adriamycin uptake; these processes may be causally linked via alterations in cytosolic calcium concentration.

CORRELATION OF THE ANTIPROLIFERATIVE ACTION OF DIPHENYLMETHANE-DERIVATIVE ANTIESTROGEN BINDING SITE LIGANDS WITH ANTAGONISM OF HISTAMINE BINDING BUT NOT OF PROTEIN KINASE C-MEDIATED PHOSPHORYLATION

Lorne J. Brandes, Jon M. Gerrard, R. Patricia Bogdanovic, Don W. Lint, Ronald E. Reid, and Frank S. LaBella

The nonestrogen receptor-mediated antiproliferative action of antiestrogen binding site (AEBS) ligands, including triphenylethylene antiestrogens and phenothiazines, has been linked to their ability to inhibit protein kinase C (PKC). Recent studies indicate that some diphenylmethane derivatives inhibit growth, are potent AEBS ligands, and antagonize histamine binding at an AEBS-related histamine site different from H_1 and H_2. Three novel diphenylmethane derivatives, N,N-diethel-2-[4-(phenylmethyl)phenoxy]ethanamine.HCl (DPPE), 4-decanoyl-DPPE (dec-DPPE), and 4-benzylphenyl decanoate (BPD) were studied in an attempt to determine whether PKC or histamine interactions best correlate with their antiproliferative effects. Platelet aggregation and the phosphorylation of a platelet M_r 47,000 protein (p47) induced by phorbol-12-myristate-13-acetate (PMA) represent two processes mediated by PKC. DPPE inhibits PMA-induced aggregation [50% inhibitory concentration (IC_{50}) = 31.2 ± 2.4 (SEM) x 10^{-6} M] but does not significantly inhibit either MPA-induced phosphorylation of M_r 47,000 protein ($IC_{50} > 500 \times 10^{-6}$ M) or binding of [^{3}H]phorbol dibutyrate to platelets, dec-DPPE is a more potent inhibitor of PMA-induced platelet aggregation ($IC_{50} = 18.8 \pm 0.7 \times 10^{-6}$ M), a weak inhibitor of M_r 47,000 phosphorylation (IC_{50} = 80-200 x 10^{-6} M), but is without effect on [^{3}H] phorbol dibutyrate binding. BPD, which lacks the alkylaminoethoxy side chain necessary for binding to the AEBS/DPPE site, is devoid of anti-PMA effects. These results are compared to the inhibition of [^{3}H] histamine binding in rat cortex membranes (K_i value for DPPE = $0.83 \pm 0.62 \times 10^{-6}$ M; K_i value for dec-DPPE = $6.6 \pm 3.5 \times 10^{-6}$ M; BPD is inactive) and growth inhibition of MCF-7 cells (IC_{50} value for DPPE = 4.5×10^{-6} M; IC_{50} value for dec-DPPE = 1.5×10^{-5} M; BPD is ineffective at all concentrations tested). Thus, while dec-DPPE is a more potent inhibitor of binding and is correspondingly more antiproliferative than dec-DPPE. The results support a relationship between antagonism of histamine binding and growth inhibition but argue against an association between the anti-proliferative effects of of DPPE and dec-DPPE and inhibition of PKC. The findings for DPPE suggest that platelet response to PMA, antagonized by diphenylmethane-type AEBS-ligands, may be mediated, at least in part, by mechanisms other than activation of protein kinase C-dependent phosphorylation.

DIRECT CORRELATION BETWEEN DNA TOPOISOMERASE II ACTIVITY AND CYTOTOXICITY IN ADRIAMYCIN-SENSITIVE AND -RESISTANT P388 LEUKEMIA CELL LINES

Abdul M. Deffie, Janendra K. Batra and Gerald J. Goldenberg

The relationship between DNA topoisomerase II activity and drug resistance was studied in cloned cell lines of Adriamycin (ADR)-sensitive and -resistant P388 leukemia; drug resistant P388/ADR/3 (clone 3) and P388/ADR/7 (clone 7) cells are 5- and 10-fold more resistant to ADR than the sensitive cell line P388/4 (Cancer Res., **46**:2978, 1986). Topoisomerase II catalytic activity in crude nuclear extracts was reduced in drug-resistant cells as determined qualitatively by decatenation of kDNA. Using the centrifugal method of quantitative analysis, topoisomerase II catalytic activity (mean ± SE) was 81 ± 10 units/mg total nuclear protein in sensitive cells, 29 ± 2 units/mg total nuclear protein in resistant clone 7 cells, these differences were highly significant ($P < 0.005$). Similarly, quantitative analysis of DNA cleavage activity using 3' ^{32}P-end-labeled pBR322 restriction fragments showed that drug-stimulated topoisomerase II cleavage activity in nuclear extracts from sensitive cells was approximately 1.7 and 2.9-fold greater than that from resistant clone 3 and 7 cells, respectively. Western blot analysis of nuclear extracts from the three cell lines using antibody against the C-terminal half of recombinant-prepared human topoisomerase II polypeptide revealed reduced immuno-reactivity of topoisomerase II protein in the drug-resistant cells. These data suggest that reduced topoisomerase II activity in resistant cells, which may represent quantitative reduction of the enzyme, may be another property contributing to multifactorial drug resistance in these cells.

MULTIFACTORIAL RESISTANCE TO ADRIAMYCIN: RELATIONSHIP OF DNA REPAIR, GLUTATHIONE TRANSFERASE ACTIVITY, DRUG EFFLUX, AND P-GLYCOPROTEIN IN CLONED CELL LINES OF ADRIANYCIN-SENSITIVE AND -RESISTANT P333 LEUKEMIA

Abdul M. Deffie, Tawfiq Alam, Charita Seneviratne, Samuel W. Beenken, Janendra K. Batra, Thomas C. Shea, William D. Henner and Gerald J. Goldenberg

Cloned lines of Adriamycin (ADR)-sensitive and -resistant P388 leukemia have been established, including P388/ADR/3 and P388/ADR/7 that are 5- and 10-fold more resistant than the cloned sensitive cell line P388/4 (Cancer Res., **46**:2978, 1986). A time course of ADR-induced DNA double-strand breaks revealed that in sensitive P388/4 cells, evidence of DNA repair was noted 4 h after removal of drug, whereas in resistant clone 3 and 7 cells repair was observed 1 h after drug removal. The earlier onset of DNA repair was statistically significant ($p = 0.0154$ for clone 3 cells, and $p = 0.0009$ for clone 7 cells). By contrast, once the repair process was initiated, the rate of repair was similar for all three cell lines.

The level of glutathione transferase activity was determined in whole cell extracts. Enzyme activity (mean ± SE) in sensitive cells was 9.49 ± 1.00 nmol/min/mg protein, that in resistant clone 3 cells was 13.6 ± 1.03 nmol/min/mg, and that in clone 7 cells was 13.96 ± 1.44 nmol/min/mg; the 1.44-fold increase in enzyme activity in resistant cells was statistically significant ($p = 0.01$). Further evidence of induction of glutathione transferase was provided by Northern blot analysis using a ^{32}P-labeled cDNA for an anionic glutathione transferase, which demonstrated approximately a twofold increase in mRNA in resistant clone 7 cells. Western blot analysis with a polyvalent antibody against anionic glutathione transferase also revealed a proportionate increase in gene product in resistant cells.

Dose-survival studies showed that ADR-resistant cells were cross-resistant to actinomycin D, daunorubicin, mitoxantrone, colchicine, and etoposide, but not to the alkylating agent melphalan; this finding provided evidence that these cells are multidrug resistant. Using a cDNA probe for P-glycoprotein, a phenotypic marke for multidrug resistance, Northern blot analysis showed an increase in the steady state level of mRNA of approximately twofold in resistant clone 3 and 7 cells. Southern analysis with the same cDNA probe showed no evidence of gene amplification or rearrangement. Western blot analysis with monoclonal C219 antibody demonstrated a distinct increase in P-glycoprotein in resistant cells.

Efflux of Adriamycin as measured by the efflux rate constant was identical in all three cell lines. Furthermore, the metabolic inhibitors azide and dinitrophenol did not augment drug uptake in either sensitive or resistant cells. These findings suggest that despite the increase in P-glycoprotein, an active extrusion pump was not operational in these cells.

This and previous studies provide unequivocal evidence that resistance to Adriamycin is multifactorial. Decreased drug uptake, decreased formation of DNA single- and double-strand breaks, increased glutathione transferase activity, earlier onset of DNA repair, as well as elevated P-glycoprotein are all characteristic of multifactorial drug resistance.

A NOVEL NON-H_1, NON-H_2 HISTAMINE ANTAGONIST PROTECTS AGAINST CYSTEAMINE-INDUCED DUODENAL ULCERS IN RATS

Gary B. Glavin and Lorne J. Brandes

A newly synthesized para-diphenylmethane derivative, N,N-diethyl-2-[4-(phenylmethyl) phenoxy]ethanamine-HCl (DPPE), binds with high affinity to the microsomal antiestrogen binding site (AEBS). Recent data suggest that the DPPE/AEBS binding site is closely related to a novel low-affinity, non-H_1, non-H_2 histamine site which may be associated with a calcium channel. We previously have shown that DPPE markedly reduces stress-induced and ethanol-induced gastric ulcers and attenuates gastric acid secretion. We now show that DPPE also profoundly reduces cysteamine-induced duodenal ulcers in rats.

ANTIULCEROGENIC AND ANTISECRETORY EFFECTS OF A NOVEL DIPHENYLMETHANE DERIVATIVE AND ANTIESTROGEN BINDING SITE LIGAND

Gary B. Glavin and Lorne J. Brandes

N,N-Diethyl-2-[4-(phenylmethyl)phenoxyl]-ethanamine hydrochloride (DPPE) is a para-diphenylmethane derivative that binds selectively and with high affinity to the microsomal antiestrogen binding site (AEBS). Recent studies with DPPE indicate that AEBS is closely related to a lower affinity non-H_1, non-H_2 histamine site that may be associated with calcium channels; the DPPE-AEBS site is different from that which verapamil binds, however, DPPE, but not verapamil, demonstrates antiproliferative effects in vitro and is antiestrogenic in vivo. We now show that DPPE profoundly inhibits restraint and cold stress and ethanol-induced gastric ulcer formation, accelerates ulcer healing, attenuates the stress-induced rise in plasma corticosterone level, and significantly reduces basal and H_2 agonist (dimaprit)-stimulated and, to a lesser extent, bethanechol-stimulated gastric acid output in conscious rats. A nonulcerogenic but prostaglandin-depleting dose of indomethacin completely blocks the inhibitory effects of DPPE on stress ulcer formation. Conversely, verapamil only slightly attenuates dimaprit-stimulated gastric acid secretion and exacerbates ethanol-induced gastric ulcers; its anti-stress ulcer effects are only partially attenuated by indomethacin. These findings support the likelihood that the site of action of DPPE is different from that of verapamil, and that an effect on prostaglandins may, at least in part, contribute to its antiulcer and apparent cytoprotective effects.

GLUTATHIONE S-TRANSFERASE, SULFHYDRYL GROUPS AND DNA CROSSLINKING ACTIVITY WITH CHLORAMBUCIL IN CHRONIC LYMPHOCYTIC LEUKEMIA

James B. Johnston, Lyonel G. Israels, Gerald J. Goldenberg, Cynthia D. Anhalt, Linda Pugh, Michael R. A. Mowat and Asher Begleiter

The glutathione levels and glutathione S-transferase activities have been measured in the leukemic cells of twelve patients with chronic lymphocytic leukemia, and correlated with the frequency of DNA crosslinks formed when the cells were incubated with chlorambucil *in vitro.* An inverse correlation was observed between the glutathione S-transferase activities and crosslinking when the data were analyzed by regression analysis. This correlation was enhanced if both glutathione S-transferase activities and glutathione levels were related to the *in vitro* crosslinking by chlorambucil, although the correlation between the glutathione levels alone with the crosslink frequency did not achieve statistical significance. There was no apparent correlation between the extent of prior exposure to alkylating agents *in vivo* and the glutathione levels or glutathione S-transferase activities. There was no obvious relationship between clinical responsiveness to chlorambucil and the *in vitro* production of crosslinking by chlorambucil. thus, glutathione S-transferase plays a major role in protecting the leukemic cell DNA from crosslinking by chlorambucil in chronic lymphocytic leukemia and this effect is enhanced by cellular glutathione. Further studies are needed to evaluate the role of chlorambucil crosslinks and their repair in the clinical sensitivity to this agent.

CHARACTERIZATION OF THE DNA-DNA CROSSLINKING ACTIVITY OF 3'-(3-CYANO-4-MORPHOLINYL)-3'-DEAMINOADRIAMYCIN

Michael I. Jesson, James B. Johnston, Erica Robotham and Asher Begleiter

3'-(3-Cyano-4-morpholinyl)-3'-deaminoadriamycin (CMA) is a highly potent analogue of the antitumor agent Adriamycin, being up to 1000 times more cytotoxic both *in vivo* and *in vitro.* In contrast to Adriamycin, CMA and 5-imino-3'-(3-cyano-4-morpholinyl)-3'-deaminoadriamycin (ICMA), its 5-imino derivative, have been shown to possess alkylating activity, as seen by their ability to produce DNA-DNA crosslinks in human and murine tumor cells and in isolated λ-phage DNA. We have compared the pharmacological activities of CMA, ICMA, and the alkylating agent chlorambucil, in an attempt to understand the roles of intercalation, the quinone ring, and DNA base composition, for crosslinking by CMA. CMA was 26-fold and 1000-fold more active than ICMA and chlorambucil, respectively, in crosslinking DNA in L5178Y cells. Similarily, CMA was 24-fold and 453-fold more active than ICMA and chlorambucil, respectively, in producing DNA crosslinks in isolated λ-phage DNA. In contrast, CMA showed only a 6-fold increase, compared to chlorambucil, in alkylating activity as measured by its ability to bind to the nucleophile p-nitrobenzyl pyridine. The Adriamycin analogues were able to intercalate into DNA in the order of CMA>ICMA, while chlorambucil did not intercalate. In addition, the intercalating agent ethidium bromide inhibited the crosslinking activity of CMA but not that of CHL, suggesting that the combination of intercalation and alkylation leads to the crosslinking activity of CMA. CMA produced an increasing level of crosslinking, but showed no difference in intercalation, in isolated DNA of increasing guanine and cytosine residues, suggesting a preference for crosslinking with G-C bases of DNA. Both the crosslinking and intercalating, but not alkylating activities of CMA and ICMA were decreased in the presence of the reducing agent, sodium borohydride. These studies suggest that the intercalative interaction of the Adriamycin analogues, CMA and ICMA, with DNA may enhance their DNA crosslinking activity. Furthermore, the quinone group may influence the intercalating activity of these agents, and thus account for the difference in crosslinking activity between CMA and ICMA.

INTERACTION OF ESTROGEN-NITROSOUREA CONJUGATES WITH THE ESTROGEN RECEPTOR IN RAT UTERUS

Hing-Yat Peter Lam, Gerald J. Goldenberg and Chiu-Ming Wong

Several estrogen-nitrosourea conjugates have been synthesized with the aim of producing more selective cytotoxic agents. The conjugates were shown to compete with estradiol for binding to cytosolic estrogen receptor in rat uterus the relative binding affinites for N-(2-chloroethyl)-N'-(3,17β-dihydroxyestra-1,3,5(10)-trien-17α-yl)-N-nitrosourea (17αCNU), N-(2-chloroethyl)-N'-(3-hydroxyestra-1,3,5(10)-trien-17β-yl)-N-nitrosourea (17β-CNU), and N-(2-chloroethyl)-N'-2,3-di(p-hydroxyphenyl)-pentanyl-N-nitrosourea (HEX-CNU) were 2, 0.4, and 0.2, respectively, using a binding affinity of 100 for estradiol. In the ligand exchange assay, cytosolic receptors preloaded with 17α-CNU and HEX-CNU were found to lose some of their estradiol (E_2) binding sites, suggesting that binding to estrogen receptor (ER) may be irreversible. An increase of nuclear accumulation of ER was observed in the presence of 17α-CNU and HEX-CNU. In the rat system, even at a 10,000-fold excess, these two agents failed to show any antagonism of the uterotrophic effect of E_2 in vivo. The low binding affinity and instability of these conjugates may account for their lack of antiestrogen activity. On the other hand, 17α-CNU at 100 or 1000 μg/day and HEX-CNU at 1000 μg/day demonstrated significant uterotrophic activity. This study did not resolve whether the stimulation of uterine growth was due to the parent estrogen-nitrosourea conjugate or to decomposition and/or metabolic products.

2'-DEOXYCOFORMYCIN IN CHRONIC LYMPHOCYTIC LEUKEMIA: CLINICAL EFFICACY AND EFFECTS ON LEUKEMIC CELL ADENOSINE DEAMINASE ACTIVITY

James B. Johnston, Asher Begleiter, Robert I. Glazer, Linda Verburg, Peter M. Venner, and Lyonel G. Israels

Twenty-three patients with refractory chronic lymphcytic leukemia (CLL) were treated with the adenosine deaminase (ADA) inhibitor, 2'-deoxycoformycin (dCF), 4 mg/M^2 i.v. weekly for 2 to 5 weeks, followed by intermittent dCF. Six patients (25%) showed a 40-87% (median 64%) decline in lymphocyte count following two injections, with subsequent improvements in neutrophil and/or platelet counts. Eight patients showed a >50% fall in peripheral lymphocyte count, but no improvements in other hematological parameters and 9 patients did not respond to treatment. The major toxicity was nausea/vomiting, which occured in 13 patients and was moderately severe in 7. Other toxicities included diarrhea, alterations in taste and lethargy. Over a cumulative period of 250 months, 10 patients had 19 espisodes of infection, which frequently occurred shortly after treatment. The pretreatment mononuclear cell ADA activities ranged from 1.6 to 64 nmol adenosine/hr/10^6 cells, which were lower than for control cells (70 to 200 nmol adenosine/hr/10^6 cell). However, neither the pretreatment ADA activities, the degree of inhibition of ADA 24 hr following dCF or the subsequent rate of recovery of ADA, correlated with clinical response. The plasma deoxyadenosine levels rose slightly following dCF, but the degree of increase did not correlate with clinical response or toxicities. Thus, with moderate toxicity, low-dose dCF may be useful in some patients with refractory CLL.

INTERACTION OF ESTROGEN-NITROSOUREA CONJUGATES WITH THE ESTROGEN RECEPTOR IN RAT UTERUS

Hing-Yat Peter La, Gerald J. Goldenberg and Chiu Ming-Wong

Several estrogen-nitrosourea conjugates have been synthesized with the aim of producing more selective cytotoxic agents. The conjugates were shown to compete with estradiol for binding to cytosolic estrogen receptor in rate uterus; the relative binding affinities for N-(2-chloroethyl)-N'-(3, 17β-dihydroxyestra-1,3,5(10)-trien-17α-yl)methyl-N-nitrosourea (17α-CNU), and N-(2-chloroethyl)-N'2,3-di(p-ohdroxyphenyl)-pentanyl-N-nitrosourea (HEX-CNU) were 2, 0, 4 and 1, 2, respectively, using a binding affinity of 100 for estradiol. In the ligand exchange assay, cytosolic receptors preloaded with 17αCNU and HEX-CNU. In the rat system, even at 10,000-fold access, these two agents failed to show any antagonism of the uterotrophic effect of E_2 in vivo. The low binding affinity and instability of these conjugates may account for their lack of antiestrogen activity. On the other hand, 17αCNU at 100 or 1000 μg/day and HEX-CNU at 1000 μg/day demonstrated significant uterotrophic activity. This study did not resolve whether the stimulation of uterine growth was due to the parent estrogen-nitrosourea conjugate or to decomposition and/or metabolic products.

C. IMMUNOLOGY/HEMATOLOGY

EVIDENCE FOR A LINK BETWEEN INOSITOL CYCLE SECOND MESSENGERS AND NATURAL KILLER (NK) CELL DEGRANULATION AND KILLING

E. A. Atkinson, J. M. Gerrard, and A. H. Greenberg

Exocytosis of cytotoxic granules towards bound tumor targets is thought to be important in NK-cell mediated killing. The biochemical mechanisms which mediate this granule mobilization are unknown, although Ca^{++} is believed to be necessary. Many other types with Ca^{++}-dependent secretory functions respond to external stimuli by activation of the inositol cycle. This cycle generates potent second messengers, most notably inotitol trisphosphate (IP_3) and diacylglycerol (DAG), from the membranephospholipid parent molecule phosphatidylinositol-4,5-biphosphate (PIP_2). IP_3 mobilizes intracellular Ca^{++}, and DAG activates the membrane-associated enzyme protein kinase C (PKC). We have previously reported activation of the inositol cycle and the generation of these second messengers in a rat large granular lymphocyte cell line functional NK characteristics (RNK) upon exposure to susceptible tumor targets. We now have evidence that these second messengers are intimately involved in NK-medicated killings at the degranulation level. Blocking IP_3 and DAG formation by binding PIP_2 with the drug neomycin dose-dependently inhibited killing of a susceptible tumor target (YAC-1) by RNK and normal rat nylon wool-nonadherent splenocytes. The PKC-activating phorbol ester PMA dose-dependently enhanced RNK killing of YAC-1. To test the hypothesis that IP_3 and DAG might be involved in NK granule exocytosis, we have employed an assay which detects the release of a granule-localized serine esterase (BLT-esterase) as a measure of degranulation. The calcium ionophore A23187, which can be used in place of IP_3 to elevate internal Ca^{++} levels caused a dose-dependent release of BLT-esterase from RNK cells. Activating PKC with PMA had little effect on degranulation of its own, but could synergize with A23187 to promote a dose-dependent release of BLT-esterase. To confirm that the released BLT-esterase detected was indeed due to a secretory event, we used heavy water or cytochalasin B, two agents which enhance secretion in other cell types, and observed a marked enhancement of BLT-esterase release. Taken together, these data lead us to propose that NK cells form IP_3 and DAG in response to susceptible target cells, and a major function of these second messengers is to mediate the exocytosis of cytotoxic granule contents toward the bound target cells.

NATURAL ANTIBODIES IN TUMOR DEVELOPMENT

Donna A. Chow

Tumor Development

Current models of tumor development must account for the clonal nature of many neoplasms and the extensive cellular heterogeneity of established tumors. The transformation of a single cell may provide a clonal origin, while the heterogeneity has been attributed to tumor progression, described by Foulds as a sequence of qualitative changes occurring over a long period of time. Although more than one event is considered necessary to produce a malignancy, the nature of the changes that lead to alterations in tumor phenotype is controversial and is likely to include mutations and changes in gene expression. Foulds proposed that, consistent with their role in normal developmental biology, regulatory mechanisms that contribute to the phenotypic alterations associated with cellular differentiation would be an essential part of neoplastic development. Nowell, however, argued that tumor progression consisted of tumor variant generation due to the acquired genetic lability of an expanding tumor population followed by selective elimination of the basis of immunological destruction or other homeostatic control mechanisms, leaving the cell with a selected advantage for survival.

Immune Resistance Against Tumors

The concept of immune surveillance proposed by Thomas and elaborated by Burnet gave the primary protective role against neoplasia to the phenomenon of homograft rejection. Subsequent testing demonstrated that the thymus-dependent adaptive immune response plays a central role in the defense against viral oncogenesis considered to be accompanied by the expression of strong tumor associated antigens. However, our early experiments suggested that the induction of an adaptive response was blocked by exposure to a small inoculum of a weakly immunogenic syngeneic murine lymphoma of non-viral origin, and following the failure of others to confirm the prediction that athymic nude mice would exhibit higher frequencies of a broad range of spontaneous tumors, the study of immune surveillance expanded to encompass the mediators of natural resistance. These thymus-independent agents include natural killer (NK) cells, the subject of extensive investigation recently; activated macrophages, which have been studied for many years and are the focus of our investigations; and natural antibodies (NAb), a relatively unexplored component of natural resistance (NR). The importance of these immunoglobulins is, however, suggested by 1) their presence in the circulation of normal, not intentionally stimulated individuals of a wide range of vertebrate species; 2) their broad ranges of specificities, including every tumor cell tested; and 3) their augmentation in response to environmental stimulation. Although their biological relevance is currently uncertain, their reactivity with effete red blood cells and aging platelets suggested a physiological role in removing cells that have ceased to function, and their recognition of tumor cells indicates that the same mechanism(s) may be effective against aberrant cells. In addition, correlative evidence obtained through the examination of different tumor lines and clones expressing disparate NAb susceptibilities, and through ontogeny studies and winn-type assays all supported a role for NAb acting against tumors in vivo.

A NOVEL MECHANISM FOR THE SELECTION OF ISOTYPE-SPECIFIC ANTIBODY RESPONSES: THE ROLE OF INTESTINAL T CELLS IN THE REGULATION OF IgA SYNTHESIS BY THE ANTI-SUPPRESSOR CIRCUIT

P. B. Ernst, J. Maeba, S. I. Lee and F. Paraskevas

Within 6 hr of immunization of mice contains a unique form of processed antigen, which consists of a complex of immunoglobulin (Ig) and antigen formed in the presence of a factor derived from the anti-suppressor inducer T cell. This complex binds to and activates the anti-suppressor effector T cell, which eventually leads to the inhibition of suppressor cell function. Both of these cells are present in the spleen (SPL) and play a role in the regulation of antibody responses. The purpose of these studies was to identify the anti-suppressor T cells in gut-associated lymphoid tissue and compare their function to their splenic counterparts. Inducer cells were detected in the Peyer's patches (PP), mesenteric lymph nodes but not in the intra-epithelial lymphocytes. The effector cells, which take up the complexes, were detected in PP and lamina propria lymphocytes but not in the intra-epithelial or mesenteric lymph node lymphocytes. Furthermore, the uptake of the complexes correlated with the presence of T cells bearing Ia antigens. The PP and SPL anti-suppressor cells were compared for their ability to enhance the production of IgA and IgG. The data clearly showed that the product of the inducer cell, and the effector cell it activates, not only enhanced the antigen-specific responses but also selected for isotope-specific antibody responses. Cells from SPL enhanced IgG greater than IgA, whereas cells from PP selected for IgA. Thus, the presence in PP of cells in the anti-suppressor circuit and their ability to selectively promote IgA synthesis suggest that this regulatory mechanism plays a significant role in intestinal immune responses.

PLATELET AGGREGATION: CELLULAR REGULATION AND PHYSIOLOGIC ROLE

Jonathon M. Gerrard

The hemostatic functions of the platelet depend in a large part on adhesion and aggregation processes. Both the proteins that mediate the adhesive processes and their cellular binding sites have been identified, with much information derived from the study of several inherited syndromes of impaired hemostasis. Implications for more effective prevention of pathologic thrombosis are stressed.

NEONATAL PLATELET FUNCTION: EVALUATING DENSE GRANULE SECRETION

Sara J. Israels

The secretion response of neonatal platelet dense graules is abnormal and is closely linked to defects in the aggregation response of these platelets. The secretion response is the result of activation of two complementary, but separable, pathways: calcium-dependent granule centralization and protein kinase C-dependent granule fusion. Using specific activators of each pathway, we evaluated the function of each pathway in the neonatal platelet as a possible cause of the poor secretion response. Neonatal platelets did not differ from adult platelets in response to stimulation of either unique pathway. However, their response to collagen, a physiologic agonist that produces activation of both pathways is markedly decreased compared to adult control platelets. This suggests that the complementary pathways resulting in secretion are intact in the neonatal platelet, but that an earlier step may be deficient, particularly one that is critical to collagen-induced activation. Ongoing studies are examining the presence and function of the collagen receptor on the plasma membrane of neonatal platelets.

MEMBRANE MICROFILAMENT INTERACTIONS IN BLOOD PLATELETS

Sara J. Israels

Platelets in association with fibrinogen, form the hemostatic plug at sites of the blood vessel wall injury. The interaction of fibrin and activated platelets form a mesh-like structure which contracts with time to allow recannulation of the vessel. This contractile process is the result of continuity of the contractile cytoskeleton of the platelet, the receptors on the membrane surface and the fibrin strands. Activation of single platelets has demonstrated redistribution of these receptors from a homogenous distribution, to clusters located largely on the extended platelet pseudopods. Our studies examine the redistribution of these receptors on platelets within a clot. Immunofluorescence studies demonstrate loss of the homogenous staining pattern as the clot contracts. This redistribution is now being examined using immuno-electron microscopy to determine whether redistribution of the reeptor is directed at sites of platelet-fibrin interaction.

INCREASES IN INTRACELLULAR CALCIUM MAY ENHANCE CYTOLYSIN-MEDIATED CYTOLYSIS OF YAC-1 LYMPHOMA CELLS

R. P. Kraut, R. Bose and A. H. Greenberg

Cytolysin, a protein derived from an present in the granules of natural killer cells, can polymerize and insert into the membranes of target cells to form pores. These pores, in large numbers, may promote Target Cell (TC) death through colloid osmotic lysis, but in small numbers may promote cell death through the derangement of Ca^{++}-dependent cellular activities. The intracellular free Ca^{++}-dependent cellular activities. The intracellular free Ca^{++} concentration, $[Ca^{++}]_i$, is normally about 1/10,000 of the extracellular Ca^{++} concentration $[Ca^{++}]_o$, and increases in $[Ca^{++}]_i$ have been linked with both cell death and activation of cellular repair mechanisms. Cytolysin polymerization and insertion are Ca^{++}-dependent processes, thus it is difficult to distinguish the role of Ca^{++} in pore formation from any role it may play in the target cell's response to cytolysin. In this regard, while Ba^{++} and Sr^{++} are highly permeant in Ca^{++} channels they cannot substitute for Ca^{++} in the polymerization of cytolysin as indicated by the pre-incubated with Ba^{++} or Se^{++}. Thus, the finding, that addition of low concentrations of Ba^{++} and Sr^{++} (1.33mM) to Ca^{++}-containing media or partial substitution of Ca^{++} with Ba^{++} or Sr^{++} gives greater cystolysin-mediated cytolysis of targets than Ca^{++} alone, may distinguish Ca^{++}-mediated pore formation from Ca^{++}-mediated derangement of cell metabolism, and indicate the importance of Ca^{++} channels in cytolysin-mediated cytolysis. Furthermore, verapamil, a blocker of voltage-gated Ca^{++} channels, inhibits Ca^{++} influx and also cytolysin-mediated cytolysis. In many types of cells $[Ca^{++}]_i$ appears to be related to $[Na^+]_i$. High $[Na^+]_o$ activated Ca^{++} efflux from the cell, while high $[Na^+]_i$ inhibits this efflux. We have found that there is more cytolysin-mediated cytolysis of YAC-1 cells in low NaC1 media made isoosmolar with N-methyl D-glucamine chloride than of YAC-1 in normal saline/HBSS media. Oubain, an inhibitor of the Na^+/K^+ pump, increases $[Na^+]_i$ and increases cytolysin-mediated cytolysis of targets. In addition, the cytotoxic effect of the Ca^{++} ionophore A23187 on lymphoid cells is Ca^{++} dependant, and we found that doses of A23187 and cytolysin which individually give low levels of kill could act synergistically to give higher levels of kill. In summary, these data suggest that cytolysin may promote cell death by increasing $[Ca^{++}]_i$.

MACROPHAGE T CELL INTERACTION. INDUCTION IN VITRO OF A MEDIATOR WITH POTENT ANTISUPPRESSOR ACTIVITY

Jeanette Maeba, S.-T. Lee and F. Paraskevas

A simple in vitro method is described for the induction of a potent mediator that interferes with suppressor cell function. The mediator consists of three easily identifable components, Ig, class II determinants and antigen, that form a unique complex similar to, or identical with, the complexes detected in vivo within 3-6 h after immunization. The formation of the antisuppressor mediator in vitro takes place in two steps: the first involves a macrophage-T cell interaction which generates an 'intermediate complex' containing antigen and class II determinants. In the second step the addition of immunochemically purified IgG from normal mouse serum to the macrophage-T cell supernate generates potent anti-suppressor activity, which is assayed by the conversion of suppression to immunity. It is suggested that the IgG interacts with the 'intermediate complex' giving rise to the final complex identical to that found in vivo 6 h after immunization. No activity is detected when IgG is added to a supernate of antigen-fed macrophages in the absence of T cells.

Furthermore, the T cells plays an additional important role in the formation of the final complexes since it restricts the source of the IgG that will generate the antisuppressor activity. In other words the antisuppressor function is detected only if the IgG matches the donor of the T cell in the Igh locus. The T cell involved in the formation of the complex is the Lyl+ subpopulation. This method should allow elucidation of the genetic, cellular and molecular mechanisms in the activation of this important T cell pathway.

FUNCTIONAL SIGNIFICANCE OF P53 ONCOGENE INACTIVATION IN ERYTHROLEUKEMIA CELL LINES: ESCAPE FROM THE ADAPTIVE IMMUNE RESPONSE

M. Mowat, G. Hicks, and D. Chow

The objective of these studies is to determine the significance and mechanmism of rearrangement of the p53 ocogene in the multistage erythroleukemia induced by Friend leukemia virus. We have previously described several erythroleukemia cell lines altered in their expression of p53 [Mowat et al. (1985) Nature, 314:633-636, Chow et al. (1987) J. of Virol., 61:2777-2781]. Some cell lines do not express p53 whereas others express a truncated p53 protein. Cell lines not expressing p53 show reduced tumor forming ability compared to the p53 expressing cell lines. We wanted to know what selective mechanism allows outgrowth of p53 non-expressing cell lines in spite of reduced tumorigenicity. To test the possibility that the loss of p53 expresion allows cells to escape the adaptive immune response, we have compared the adaptive stimulation and susceptibility to the immune response between p53 expressing and non-expressing cell lines isolated from the same mouse. We have found the p53 non-expressing cell line, with rearrangement of both alleles of the p53 gene, stimulates poorly as well as being less susceptible to splenic cytolysis compared to the p53 expressing cell line. This cytolysis was due to T-lymphocytes. We will be reporting on other matched sets of cell lines. To understand the mechanism of p53 gene arrangements, we have cloned both alleles of the p53 gene from one cell line. We have found insertion of sequences related to the helper virus FMULV into both alleles of p53. We will be presenting detailed molecule analysis of these clones. These results indicate that inactivation of an oncogene may also play a role in tumor progression.

INHIBITION OF ANTISUPPRESSION BY THE ACUTE MURINE GRAFT-VIRUS-HOST REACTION

Frixos Parasekvas, John Gartner, Jeannette Maeba and Sho-Tone Lee

Profound suppression of both humoral and cell-mediated immunity is a significant systemic effect of graft-versus-host reactions. Although no complete explanation has been advanced for this immunosuppression suppressor cells have been implicated. The data presented in this paper indicate that acute GVH reactions in (C57BL/61 x A/J) F_1-hybrid mice induced by the injection of A/J cells severly disrupts the function of the antisuppressor T-cell pathway at both its induction and effector stages. Results show that within 3 weeks of induction of the reaction, $Ly1^+$-T antisuppressor inducer cells lose their ability to generate the serum factor that mediates antisuppression. This factor is normally taken up by and activates $Ly2^+$ cells which then inhibit suppressor T-cell function. The data also reveal that $Ly2^+$ cells collected 2 weeks after induction lose their ability to be activated by the antisuppressor factor produced in normal mice. These cells are thus unable to function as antisuppressor effector cells. The uptake of the antisuppressor factor by $Ly2^+$ T cells depends on the expression of Ia antigens on the surface of these cells. Experiments have shown that these antigens are absent from the surface of T cells derived from mice with GVH reactions, This finding may provide an explanation for the inability of these cells to function as antisuppressor effectors. Antisuppression is an important T-cell pathway that is intimately associated with the regulation of immune function. It is possible that the immunosuppression arising in mice with GVH reactions may stem, in part, from unopposed suppressor T-cell activity that results from widespread interference by the reaction with apathway that normally inhibits suppressor cell activity.

HUMAN LAK (LYMPHOKINE ACTIVATED KILLER) CELL GRANULES CONTAIN A MACROPHAGE ACTIVATING FACTOR (MAF) THAT ACTIVATES MACROPHAGE H_20_2 PRODUCTION AND TUMORICIDAL ACTIVITY

Eugene Roussel and Arnold H. Greenberg

Recent work from our laboratory identified a MAF in the granules of a large granular lymphocte (LGL) leukemia. To verify that this MAF was present in the granules of normal human cells, we examined human LAK cell granules. Human peripheral blood lymphoctes were incubated 6 days with irradiated EBV transformed cell line 8866 and then expanded for 3 days in presence of 10μ/ml of rhIL-2. More than 95% of the cell population obtained were LGL by morphology; 50% were $CD16^+$ and 50% CD^3. Human-LAK cell granules were isolated from disrupted cell homogenate by Percoll gradient gractionation. When CSF-1 differentiated murine bone marrow-drived mϕ were incubated 9 hr with LAK cell granules, they were fully activated for lysis of the P815 tumor target cells. Optimum MAF recovery was observed when granules were solubilized in 2 M salt. Human granule-MAF was 2-3 times more potent using a bone marrow-derived Mϕ population differentiated in presence of 10-50 μ/ml rhIL-1β. The MAF showed a synergistic effect with rhIL-1β, rMuIFN-γ, and possibly rMuTNF-α. Finally, solubilized human LAK cell granules stimulated H_20_2 production from proteose peptone elicitated murine peritoneal mϕ. This work indicates that human LGL granules contain a factor capable of activating mϕ.

TUMOR PROGRESSION *IN VITRO:* TUMOR-PROMOTOR-INDUCED REVERSIBLE DECREASE IN NATURAL IMMUNE SUSCEPTIBILITY

Paul A. Sandstrom and Donna A. Chow

Growth of established murine tumor lines in media containing the phorbol ester tumor promoter 12-0-tetradecanoylphorbol-13-acetate (TPA), was associated with reversible reductions in sensitivity to *in vitro* and *in vivo* parameters of natural resistance. L5178Y-F9 cells exposed to 100 ng TPA/ml for 2 days and returned to culture without TPA for 0-2 days, exhibited reductions in sensitivity to complement-mediated lysis by natural antibodies (NAb), activated macrophages and hypotonic lysis. The natural killer (NK) cell sensitive SL2-5 lymphoma was less sensitive to NK cells, complement-dependent NAb and hypotonic lysis after 2 days growth in 2 or 3 βg TPA/ml. Although TPA-treated L5178Y-F9 cells could acquire higher levels of serum NAb *in vitro*, this was complicated by the instability of the binding at 37°C, resulting in an effectively reduced capacity to bind NAb which was also demonstrated by TPA-treated SL2-5 cells. The tumor frequency of threshold s.c. inocula and the i.v. metastatic potential of the TPA-treated tumors was increased in syngeneic DBA/2 mice revealing possible correlations between reductions in the cellular characteristics assayed *in vitro* and decreased susceptibility to host-mediated defenses *in vivo*. Continued growth of the TPA-treated cells of a total of 2-8 days without TPA produced a reversal in the *in vitro* parameters, in the tumor frequency and in the metastatic potential, indicating the requirement for TPA to maintain the resistant phenotype. These data are consistent with the initial reversible nature of the promotion phase of multistage carcinogenesis. The reversible TPA-induced reductions in sensitivity to mediators of natural resistance may be an integral component of promotion, contributing to tumor survival *in vivo* and increasing the probability that the tumor will progress to a more malignant phenotype.

TUMORIGENICITY OF MURINE LYMPHOMAS SELECTED THROUGH FLUORESCENCE-DETECTED NATURAL ANTIBODY BINDING

David F. Tough and Donna A. Chow

Fluorescence-activated cell sorting was used to isolate high and low IgM natural antibody (NAb) binding populations from a heterogeneous line of the L5178Y-F9 murine lymphoma. The ranking of NAb binding and complement-dependent NAb lysis of the selected and starting lines were the same and opposite to that of their tumorigenicity in syngeneic DBA/2 mice. L5178Y-F9 and SL2-5 clones repeatedly treated with the tumor promotor 12-0-tetradecanoylphorbol-13-acetate and selected by fluorescence-activated cell sorting for high NAb binding exhibited increases in NAb binding and sensitivity to complement-dependent NAb lysis which corresponded with reduced tumor frequencies of threshold inocula. Although the high NAb binding SL2-5 line was slightly more sensitive to natural killer (NK) cell cytolysis, changes in sysceptibility to activated macrophages or hypotonic lysis were not consistent with the observed reductions in tumor frequency so that the selected alterations in NAb binding corresponded best with tumorigenicity. These data confirm the same inverse relationship exhibited previously by *in vivo* and *in vitro* selected tumor variants and provide more precise evidence supporting a role for NAb in host resistance against tumor foci.

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M. Tenenbein and S. J. Israels. Early coagulopathy in severe iron poisoning. J Pediatr, **113**:695, 1988.

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B. Weinerman, J. Maroun, D. Stewart, C. Cripps, and J. B. Johnston. Sequential methotrexate (M), 5-fluorouracil (F) and Leucovorin (L) in metastatic measurable colorectal cancer (CRC). Does it work? Proc Am Assoc Cancer Res, **7**:102, 1988.

LIBRARY

Librarian — *Donna Chornenki*

The Library of the Manitoba Cancer Treatment and Research Foundation provides information services for the Medical Clinics and Departments in The Foundation, and The University of Manitoba's Institute of Cell Biology. Information is in support of patient care and treatment, education, and research. The Library is located on the second floor of the Foundation and occupies 1300 square feet of space.

The Manitoba Cancer Treatment and Research Foundation Library houses the largest source of oncology literature and information in the Province of Manitoba. Computerized literature searches are provided on demand to supply information, lists of references to published literature and full test retrieval of articles or book paragraphs. The data bases searched cover fields in medicine and biomedicine, toxicology, chemical abstracts, registry of toxic effects of chemical substances, state-of-the-art cancer treatment information, an International cancer research data bank, and health planning and administration.

For the year of 1988 the Library requested a total of 379 Interlibrary loans, the majority of these from the Canada Institute of Science and Technical Information in Ottawa. A total of 326 Interlibrary loans were filled by the Foundation Library, the majority of these being local lending to Hospitals and Physicians in Manitoba.

The Library's holdings at the end of 1988 were 3,317 books, 3,059 bound journals, and 87 active subscriptions to journal material. The Library also houses a complete collection of Cumulated Index Medicus from 1960 to date, as well as many serial titles.

The development of the book and journal collection is carefully monitored so that all the departments requirements and discipline interests are appropriately and proportionately represented. This is accomplished by all departments having representation on the Library Committee which meets regularly to discuss and decide on collection renewal.

VOLUNTEER SERVICES

COORDINATOR: *Elaine Hickerson, B.A.*
SECRETARY: *Anneliese Friedle*

One hundred and sixty-four volunteers worked 12,912 hours in 1988. Fifty-two new volunteers, including eleven new students were given orientation and training. New orientation kits were prepared for both Cancer Society and Cancer Foundation volunteers. Refreshment volunteers served 56,028 patients and family members. A pilot project was begun for Information Services in the fall of 1988. These additions brought the total of placement areas to twenty-seven. In addition to these regular service positions, there are volunteers who knit finger puppets, sew turbans and provide knitting for the Christmas Hampers. Their hours are unrecorded.

Learning opportunities have been offered throughout the year. Pat Edward spoke on "Breast Self Examination." Audrey Mutter spoke on "Jeffreys Folks." One volunteer and the coordinator attended the M.H.O. Conference.

Twenty-two student volunteers worked during the summer of 1988. Student volunteers assisted during the spring and Christmas vacation periods as well.

Three volunteers have given over one thousand hours of volunteer service — Ella Adams, Rosella Genik and Kay LeFevre.

The annual volunteer recognition tea was held in April. Mr. Robert Best, Chairman of the Cancer Society Board and Dr. W. McDiarmid, Chairman of the Cancer Foundation Board, spoke words of appreciation.

Honoring twenty-five years of the Refreshment Service, the Cancer Society hosted a coffee party on May 17th. Special tribute was paid to three original volunteers who are still involved on a regular basis — Ella Adams, Ressa Tod and Myrtle Weir. Spares Helen Scoble and Mae Chatfield and recently retired servers Alla Lockhart and Olive Simpson were also honoured.

Bonny Kahanovitch, convenor of our Refreshment Service was presented with a special award at the Canadian Cancer Society, Manitoba Division, annual dinner on December 1st.

The newsletter was published four times in 1988. Our volunteer editor has been with us since November 1985. Our volunteer service was featured in the summer edition of the Volunteer Centre newsletter "Network".

Twenty-four Christmas Hampers and two gift packages were prepared by volunteers. Staff and community groups continued to provide generous support. Donations totalling $882.50 were received from the Manitoba Association of Health Care Professionals, the Transcona Optimists, the Patricia Chapter, O.E.S. and individual donors.

Volunteer Services will continue to grow and change in 1989, in order to meet the needs of the patients and staff at the Cancer Foundation.

VOLUNTEERS 1988

George Ackerman
Ella Adams
Judi Adams
Terry Adams
Livvy Aftanas
Kay Ahoff
Monica Allison
Paul Bergman
Audrey Bird
Thelma Bird
Clara Black
Margaret Bonar
Margaret Booth
Mary Bosman
Bonnie Bowcott
Marjorie Brotheridge
Marion Burwash
Laura Buss
Mary Carey
June Carter
Mae Chatfield
Tammy Chesley
Melita Chick
Ethel Coakes
Crystal Contois
Edna Convey
Robert Corden
Grace Corder
Michelle Coulombe
Fran Crowston
Marj Currie
Lillian Danish
Marci Davis
Jim Diehl
Michelle Du
Betty Ellis
Ann Falk
Gina Garcia
Mildred Garvey
Rosella Genik
Cecile George
Noreen Gillanders
Esther Ginpil
Gita Glass
Cathy Hamm
Norma Haslam
Chi Hoang
Mary Inkster
Kim Irving
Julie Isleifson
Ina Jablonski
Ella Jack
John Jack
Kathy Jackson
Lorraine Jenkins
Norma Jones
Bonny Kahanovitch
Susan Keller
Hazel Klemas
Shirley Kowalchuk
Karl Kroeker
Wendy Kwan
Emma Lamb
Jocelyne Lang
Liz Lankhout
Noel Larocque
Kay LeFevre
Jill Leggett
Gayle Levesque
Irene Levinson
Lana Lupky
Margaret MacLeod
Peggy Mahon
Doris Mahoney
Marla Mainer
Anne Mackay
Rose Manchulenko
Kayla Mandshein
Maila Maranan
Rose Marier
Lorna Marshall
Mary Martens
Henrietta Martin
Fran Mason
Bev Mathieson
Esther McCubbin
Marnie McDonald
Alice McIntosh
Kathleen McKay
Heather McLean
Mary Louise McKenzie
Violet McKenzie
Alice McLennan
Margaret Mestery
Connie Meunier
Olga Miguez
Susan Milimac
Dora Moir
Doreen Morris
Jean Morrison
Emily Murphy
Kerry Mushumanski
Phyllis Nazeravich
Anne Neal
Netta Nicholson
Darlene Nickel
Alix Nicolson
Cass Nicolson
Madalina Oprea
Monelle Oman
Doreen Pauls
Bernice Peichl
Adair Phelps
Shirley Poole
Angie Popowich
Barbara Prosser
Norah Quinton
Dorothy Rankin
Jackie Reid
Giselle Robin
Kay Rokala
Julie Ruhlen
Sarah Runions
Inez Salter
Sheila Sampson
Anita Saxena
Helen Scoble
Robert Schaepe
Todd Sheppard
Lorraine Shields
Jackie Sicotte
Sheryl Singer
Margaret Slater
Dorothy Sly
Vera Smeaton
Christine Sorko
Evelyn Stanley
Jean Stewart
Mike Stolle
Anil Sud
Gill Sunderjit
Terry Sveinson
Margaret Swayze
Lorraine Tennant

Blanche Thomson
Ressa Tod
Betty Todd
Dierdre Tomkins
Kerri Tomy
Daisy Tooth
Merle Trotman
Fannie Unrode
Helen Vidal
Merl Voakes
Olive Wagner
Lynn Waller
Trudy Waller
Laurie Watts
Shelley Watts
Joan Wazny
Myrtle Weir
Sandra Whitehead
Brent Wilde
Corinne Wilson

THE CANADIAN CANCER SOCIETY PATIENT SERVICES PROGRAM

New initiatives highlighted the Patient Services Program of the Canadian Cancer Society, Manitoba Division, in 1988.

The Society committed itself to a wide-ranging study of 'The Needs of People Living With Cancer.' In Manitoba alone, 800 interviews will be conducted with cancer patients ranging from 18-80 years of age. The study, also conducted in Prince Edward Island and Quebec, is designed to identify the unmet needs of the cancer patient and the emotional and physical effects these unmet needs have on the patient. Manitoba Division will be examining the results of the study closely to determine ways of improving existing services provided by the Society.

A new pilot support group program was also conducted in 1988, for children of parents with cancer. Called 'Kids Can Cope,' the project was a joint effort by the Manitoba Cancer Treatment and Research Foundation, St. Boniface General Hospital and the Canadian Cancer Society, Manitoba Division. The pilot project involved 16 children, seven to 18 years of age, with the six-week program aimed at providing a supportive, sharing environment and educating the children about cancer and its treatment. The Society provided transportation and after-school snacks. Based on the results of the pilot project an ongoing program is planned for 1989.

The ongoing volunteer services provided by the Canadian Cancer Society continue to enhance the quality of life of cancer patients throughout Manitoba.

Lennox Bell Lodge — Cancer patients from rural Manitoba who must stay in Winnipeg to undergo treatment find convenient economical accommodation at the Lodge which occupies two floors adjoining the Manitoba Cancer Treatment and Research Foundation. As the Lodge operates at near capacity, it is recommended that advance bookings are made.

Volunteer Driver Program — Just getting to and from scheduled treatments can be traumatic. Cab fares add up quickly, and it's easy to feel like a burden to family and friends. The Volunteer Driver Program provides about 50 rides a day to people on treatment.

Reach to Recovery from Breast Cancer — Providing one-to-one visits on request, volunteer visitors, who have experienced breast cancer themselves, offer emotional support to mastectomy patients.

CanSurmount — Trained CanSurmount visitors provide emotional support, through individuals, to newly-diagnosed cancer patients. The difficulties ahead may seem insurmountable, but a CanSurmount volunteer can help because he or she offers the unique advantage of having shared the experience. CanSurmount visitors also visit informally in three treatment areas of the clinic: chemotherapy, radiotherapy, and the head and neck clinic.

Refreshment Service — Spending time in waiting rooms is made less of an ordeal by Refreshment Volunteers, who provide smiles and snacks to over 5,000 patients and their families each month.

Wig Service — Over 1,000 refurbished wigs are available free of charge at the Foundation. Turbans and scarves are also available. All children are provided with a new wig, at no cost.

Jeffrey's Folks — This support group assists the parents of children with cancer through a difficult and stressful time. The emotional support, information and friendship that this group provides is designed to alleviate the confusion and sense of isolation.

The New Voice Club — Those patients needing a laryngectomy, or who have just undergone this surgery, the support and assistance from members of The New Voice Club can help patients face the challenges ahead.

Financial Assistance Program — Established with the philosophy that no patient miss treatment due to financial difficulties, the assistance program covers the cost of accommodation, transportation or bus fare for rural patients.

GRANTS FOR RESEARCH AWARDED BY THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION FOR 1988/89

OPERATING GRANTS

E. Baral
The Effect of Estradiol and Tamoxifen on Lymphocyte reactions in Vitro

N. W. Choi
An International Collaborative Case-Control Study of Brain Tumours

J. Wright
Growth factors and myogenesis

L. J. Brandes
Study of the antiproliferative effects of DPPE, a novel histamine antagonist

EQUIPMENT

F. Paraskevas

POSTDOCTORAL FELLOWSHIPS

Dr. Lois Schwarz

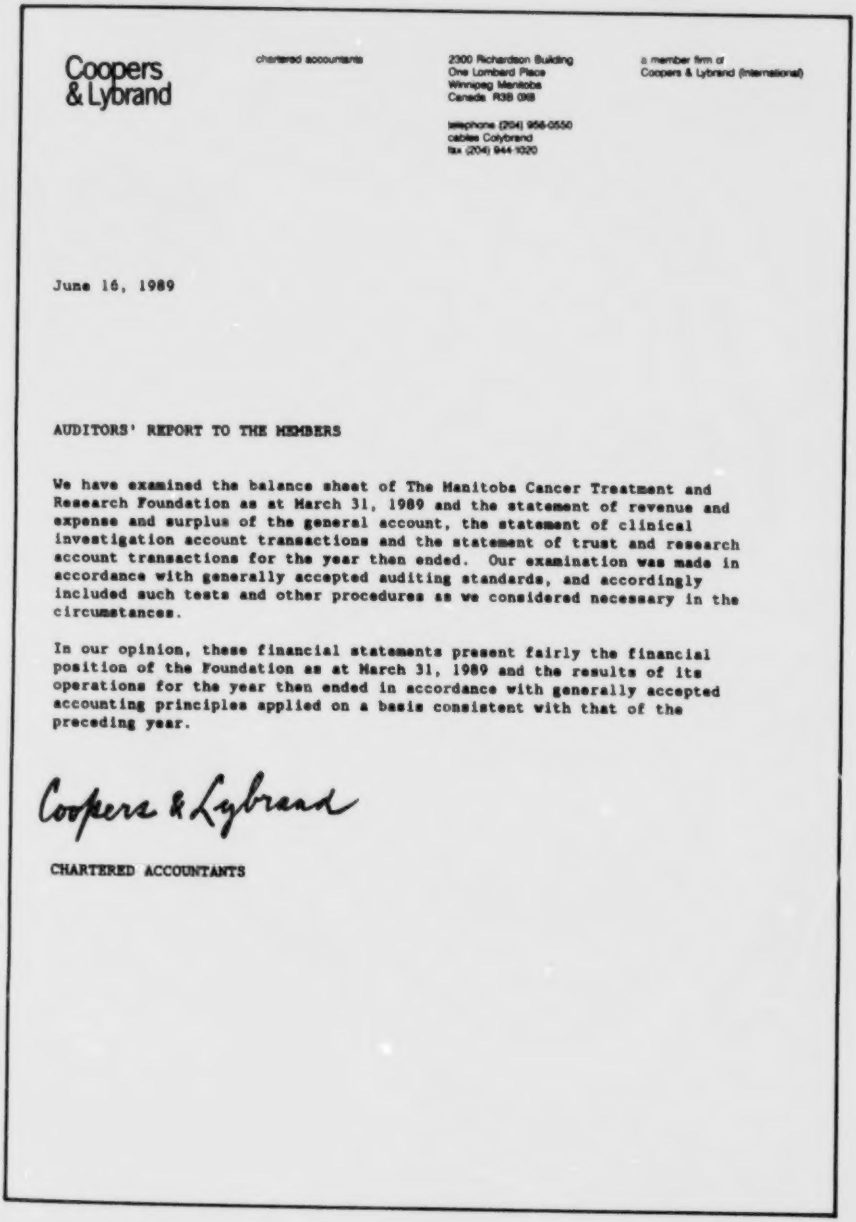
STUDENTSHIPS

P. Sandstrom
T. Chu
W. Yang
K. Chantziantoniou

CAREER AWARDS

A. Begleiter
D. Chow
P. Lam
M. Mowat

AUDITOR'S REPORT
TO THE MEMBERS
FOR THE YEAR ENDING
MARCH 31, 1989



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a member firm of
Coopers & Lybrand (International)

June 16, 1989

AUDITORS' REPORT TO THE MEMBERS

We have examined the balance sheet of The Manitoba Cancer Treatment and Research Foundation as at March 31, 1989 and the statement of revenue and expense and surplus of the general account, the statement of clinical investigation account transactions and the statement of trust and research account transactions for the year then ended. Our examination was made in accordance with generally accepted auditing standards, and accordingly included such tests and other procedures as we considered necessary in the circumstances.

In our opinion, these financial statements present fairly the financial position of the Foundation as at March 31, 1989 and the results of its operations for the year then ended in accordance with generally accepted accounting principles applied on a basis consistent with that of the preceding year.

Coopers & Lybrand

CHARTERED ACCOUNTANTS

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

BALANCE SHEET AS AT MARCH 31, 1989

ASSETS

	1989 $	1988 $
	GENERAL ACCOUNT	
Cash and term deposits	936,239	766,159
Amounts owing by the Manitoba Health Services Commission (note 2)	178,530	314,035
Accounts receivable	4,725	14,629
Amounts receivable from Clinical Investigation Account	19,700	13,371
Amounts receivable from Trust and Research Account	1,190	-
Inventory of supplies - at cost	41,549	38,422
Prepaid expenses	32,551	29,313
Equipment - at nominal value	1	1
	1,214,485	1,175,930
	CLINICAL INVESTIGATION ACCOUNT	
Cash and term deposits	277,408	392,404
Accounts receivable	550	4,288
	277,958	396,692
	TRUST AND RESEARCH ACCOUNT	
Cash	38,155	515,547
Accounts receivable and accrued interest	194,073	148,608
Amounts receivable from General Account	-	38,005
Investments - Schedule A	7,634,133	6,446,356
Deferred fundraising expense (note 5)	38,639	-
	7,905,000	7,148,516

SIGNED ON BEHALF OF THE FOUNDATION

McMullen

Member

Member

LIABILITIES

	1989 $	1988 $
Accounts payable and accrued liabilities	513,649	494,612
Amounts payable to Trust and Research Account	-	38,005
	513,649	532,617
Surplus	700,836	643,313
	1,214,485	1,175,930

Accounts payable	56,991	36,075
Amounts payable to General Account	19,700	13,371
Commitments payable	201,267	347,246
	277,958	396,692

Accounts and grants payable	189,596	203,241
Amounts payable to General Account	1,190	-
Research fund	7,714,214	6,945,275
	7,905,000	7,148,516

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

GENERAL ACCOUNT

STATEMENT OF REVENUE AND EXPENSE AND SURPLUS

FOR THE YEAR ENDED MARCH 31, 1989

	1989 $	1988 $
REVENUE		
Manitoba Health Services Commission	8,411,426	7,812,317
Recoveries from other institutions	68,054	54,610
	8,479,480	7,866,927
EXPENSE		
Operating expenses -		
Salaries and benefits	6,730,376	6,435,344
Building occupancy	682,808	672,263
General expenses	440,553	421,127
Supplies and other departmental expenses	224,626	192,294
Diagnostic services	217,429	179,179
	8,295,792	7,900,207
Equipment purchases	159,626	120,448
	8,455,418	8,020,655
EXCESS OF REVENUE OVER EXPENSE (EXPENSE OVER REVENUE)	24,062	(153,728)
DEFICIT RECOVERABLE FROM MANITOBA HEALTH SERVICES COMMISSION	-	153,728
	24,062	-
OTHER INCOME - net of unfunded costs (note 3)	33,461	6,859
SURPLUS FOR THE YEAR	57,523	6,859
SURPLUS - BEGINNING OF YEAR	643,313	636,454
SURPLUS - END OF YEAR	700,836	643,313

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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

STATEMENT OF CLINICAL INVESTIGATION ACCOUNT TRANSACTIONS

FOR THE YEAR ENDED MARCH 31, 1989

	1989 $	1988 $
RECEIPTS		
Grants received	1,115,707	698,341
Interest	22,477	26,847
	1,138,184	725,188
DISBURSEMENTS		
Artificial Intelligence Project	419,619	13,797
Associated Institutions - salary support	277,132	256,390
On-line portal imaging	109,117	-
Clinical Investigation Office	100,724	-
Lung cancer studies	62,872	42,063
Breast screening program	58,390	42,461
Theraplan modification	56,564	-
Electron Dosimetry	37,497	41
Experimental hyperthermia	23,836	18,709
Terry Fox career awards	23,254	49,192
The effect of Estradiol and Tamoxifen on Lymphocytes	19,885	-
Breast cancer adjuvant studies	-	52,989
Lonidamine - hypernephroma	-	38,762
Computer imaging	-	28,281
Other studies	68,311	106,516
Administrative costs	26,962	25,186
	1,284,163	674,387
EXCESS OF RECEIPTS OVER DISBURSEMENTS (DISBURSEMENTS OVER RECEIPTS)	(145,979)	50,801
COMMITMENTS PAYABLE - BEGINNING OF YEAR	347,246	296,445
COMMITMENTS PAYABLE - END OF YEAR	201,267	347,246

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

STATEMENT OF TRUST AND RESEARCH ACCOUNT TRANSACTIONS

FOR THE YEAR ENDED MARCH 31, 1989

	1989 $	1988 $
REVENUE		
Donations - Schedule B	444,289	915,201
Investment income	712,996	602,999
Transfer from General Account	13,250	41,000
	1,170,535	1,559,200
EXPENSE		
Research grants and personnel awards	250,878	273,460
Cell Biology	92,644	96,622
Equipment	15,029	29,758
Staff co-ordinator	25,750	24,000
Miscellaneous	17,295	9,132
	401,596	432,972
EXCESS OF REVENUE OVER EXPENSE	768,939	1,126,228
FUND BALANCE - BEGINNING OF YEAR	6,945,275	5,819,047
FUND BALANCE - END OF YEAR	7,714,214	6,945,275

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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

NOTES TO FINANCIAL STATEMENTS

FOR THE YEAR ENDED MARCH 31, 1989

1. SIGNIFICANT ACCOUNTING POLICIES

General Account

Equipment

Annual expenditures for equipment acquisitions are charged directly to operations.

Revenue

Revenue received from the Manitoba Health Services Commission for net insured patient costs is based on operating budget amounts approved annually and adjusted for amounts to be returned to or recovered from the commission in respect of surplus or deficit arising in the current fiscal year.

Surplus and deficit

The Foundation is entitled to retain surpluses arising from excess of revenue over approved expenses for each fiscal year up to a maximum of 2% of the net insured patient costs. Any surplus amount in excess of the maximum is returned to the Manitoba Health Services Commission.

The Foundation may recover deficits arising from excess of approved expense over revenue by making application to the Manitoba Health Services Commission.

Clinical Investigation Account

Basis of presentation

The Clinical Investigation Account segregates grants received from external sources for specific clinical research projects undertaken by the Foundation. Grants received and disbursements made are recorded on a cash basis. The duration of these projects usually ranges from one to three years.

Trust and Research Account

Investments

Investments are recorded at cost with any premium or discount being amortized over the term of the investment.

Investment income is recorded on the accrual basis.

Grants

Grants are included in the expenditures of the Trust and Research Fund in the year they are approved.

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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

NOTES TO FINANCIAL STATEMENTS

FOR THE YEAR ENDED MARCH 31, 1989

2. TRANSACTIONS WITH THE MANITOBA HEALTH SERVICES COMMISSION

In addition to the receipt of operating revenue, the Foundation had the following transactions with MHSC during the year:

	$	$
AMOUNTS OWING BY MHSC - BEGINNING OF YEAR		
1986 deficit recoverable	24,801	
1987 deficit recoverable	88,601	
1988 deficit recoverable	153,728	
Equipment purchases recoverable	46,905	314,035
Current year equipment purchases recoverable		159,626
Equipment purchases recovered		(181,732)
1986 deficit recovered		(19,970)
1987 deficit recovered		(76,448)
1986 and 1987 deficits not recovered and charged against other income (note 3)		(16,981)
AMOUNTS OWING BY MHSC - END OF YEAR		178,530

The 1988 net deficit of $153,728 has been recorded as receivable from MHSC. The recovery of the outstanding balance as at March 31 is subject to final audit by MHSC.

3. OTHER INCOME - net of unfunded costs

	1989 $	1988 $
Interest	66,210	63,909
Additional contributions to pension plan	-	(10,986)
Transfer to Trust and Research Account	(13,250)	(41,000)
Building renovations	-	(5,064)
Adjustments to amounts owing by MHSC	(16,981)	-
Other expenses	(2,518)	-
	33,461	6,859

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THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

NOTES TO FINANCIAL STATEMENTS

FOR THE YEAR ENDED MARCH 31, 1989

4. OBLIGATION UNDER LEASE AGREEMENT

The Foundation entered into a three year lease agreement with First City Capital Ltd. to finance the purchase of computer equipment and maintenance totalling $759,452 for the Artificial Intelligence Project in the Clinical Investigation Account. Certain leasing costs associated with the agreement were to be recovered from the International Artificial Intelligence group of Nexa Corporation who were also participating in the project. Regular lease payments were made by the Foundation until November, 1988 at which time the Foundation ceased making payments because Nexa Corporation had declared bankruptcy and was no longer contributing to the project.

The following is a summary of the anticipated payments as provided under the lease:

	$
Year ending March 31, 1989	51,820
1990	310,920
1991	259,100
Balance of lease obligation	621,840

The Foundation is currently involved in discussions with First City Capital Ltd. in an attempt to reach a settlement on the lease. It is not possible at this time to assess the outcome of these negotiations.

5. SUBSEQUENT EVENT

On May 1, 1989, the Foundation initiated a fundraising campaign aimed at the expansion of existing facilities. Certain costs associated with this fundraising campaign were incurred prior to March 31, 1989. They have been recorded as deferred expenses on the balance sheet and will be expensed in the subsequent year when fundraising revenues are received.

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SCHEDULE A

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

TRUST AND RESEARCH ACCOUNT

SCHEDULE OF INVESTMENTS AS AT MARCH 31, 1989

	Book value $	Market value $
Bonds, debentures and guaranteed investment certificates -		
B.C. Telephone Company -		
9 7/8%, November 1, 2003	50,000	44,813
Barclays Bank of Canada -		
9.60%, June 8, 1989	600,000	600,000
Bell Canada Enterprises Inc. -		
11 5/8%, May 2, 1990	251,307	251,299
Canada Trust -		
10 1/8%, December 2, 1989	100,000	100,000
City of Edmonton -		
12.875%, June 13, 1992	25,724	26,902
12.875%, December 13, 1992	73,384	74,450
Ford Credit Canada Ltd. -		
10 1/4%, March 4, 1991	99,896	97,800
Government of Canada -		
9.70%, July 28, 1989	318,529	318,529
10 1/4%, September 1, 1989	289,341	284,969
12 1/4%, November 1, 1989	100,000	99,700
9 3/4%, May 1, 1991	199,086	195,423
10 7/8%, November 1, 1991	29,943	29,074
9 1/4%, July 1, 1992	198,209	189,500
10.93%, November 1, 1992	85,371	82,745
10 3/4%, May 1, 1993	453,191	450,896
9 1/4%, May 15, 1997	200,000	185,500
Government of Canada Treasury Bills -		
9.20%, April 28, 1989	458,426	458,426
10.10%, August 4, 1989	185,896	185,896
11.40%, September 8, 1989	74,861	74,861
Investors Group Debentures -		
9 7/8%, October 4, 1998	50,000	46,063
Carried forward	3,843,164	3,796,846

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SCHEDULE A
Page 2

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

TRUST AND RESEARCH ACCOUNT

SCHEDULE OF INVESTMENTS AS AT MARCH 31, 1989

	Book value $	Market value $
Brought forward	3,843,164	3,796,846
Bonds, debentures and guaranteed investment certificates (cont'd) -		
Metropolitan Trust -		
10 1/4%, June 27, 1989	48,962	48,962
Montreal Trust -		
9.70%, July 21, 1989	300,000	300,000
11 1/4%, October 2, 1990	20,000	20,000
National Trust -		
10 1/2%, September 26, 1989	200,000	200,000
10 1/8%, December 4, 1989	70,000	70,000
Ontario Hydro Bonds -		
10 3/4%, December 15, 1992	199,453	199,878
9 3/4%, January 15, 1993	596,475	581,147
9 1/2%, February 10, 2000	400,000	372,000
Royal Bank of Canada -		
10%, December 1, 1994	160,000	150,400
Royal Bank Mortgage Corporation -		
9 3/4%, October 10, 1989	175,000	175,000
9 3/4%, October 1, 1989	25,000	24,750
Royal Trust -		
10.13%, July 29, 1989	500,000	500,000
10 1/4%, December 19, 1990	150,000	150,000
9 5/8%, May 1, 1991	10,000	10,000
11 1/4%, December 13, 1993	225,028	225,028
11.38%, December 19, 1993	500,000	500,000
11%, December 21, 1993	10,005	10,005
10.9%, August 15, 1994	201,046	200,000
	7,634,133	7,534,016

SCHEDULE B

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION
TRUST AND RESEARCH ACCOUNT
SCHEDULE OF DONATIONS
FOR THE YEAR ENDED MARCH 31, 1989

	$
UNRESTRICTED DONATIONS	
Non-designated	
Estate William R. Adley	1,570
In memory of Thomas Lorne Allan	576
Estate Stephanie Archaire	3,000
Donation BA Employee Charitable Fund	500
In memory Herbert Best	560
Donation Mr. & Mrs. J.E. Best	500
Estate Grace Weir Birch	500
Donation Joe Brain Foundation	25,000
Donation Building Products & Concrete	600
Estate Eva Calverly	24,261
Donation Canadian Tire	1,000
Estate of Eunice Crookshanks	13,600
In memory of Terry Fox	120
Estate of Anne Froese	1,040
In memory of Lyn Gibson	1,000
Estate Frances Gilbert	979
Estate Ingun Gillie	500
Donation Bill Golke	1,000
Donation Miss Elizabeth Grierson	500
In memory of Lloyd Gunnlaugson	670
Donation Health Sciences Centre Employees Charitable Fund	2,429
In memory of Robert R. Hodgson	525
In memory of John Hrabchuk	720
Donation William J. Irmie	1,000
In memory of Dorothy E. James	773
In memory of Vera Kleiner	1,035
In memory of Alfred Lalonde	538
In memory of James Archibald Leitch	500
In memory of Kenneth Lord	524
Donation Esther Maizlen	500
Donation Manitoba Hydro Employees	1,300
In memory of Joseph L. Matthews	500
Donation Meyers, Norris, Penny & Co.	1,000
In memory of Christine Michalchyshyn	913
In memory of Ralph Mitchell	500
Estate of Leo J. Morin	60,178
In memory of Ruby Neuman	905
Estate of G.O. Ortwin	2,000
Donation Mrs. K. Quintaine	500
Estate of Phyllis M. Rea	9,000
Donation Joseph Sharp	500
Estate of Lorraine L. Shields	3,788
In memory of Albert Singer	674
Estate of Lillian C. Smith	728
In memory of Margaret Smith	1,570
Carried forward	170,076

Coopers & Lybrand

SCHEDULE B
Page 2

THE MANITOBA CANCER TREATMENT AND RESEARCH FOUNDATION

TRUST AND RESEARCH ACCOUNT

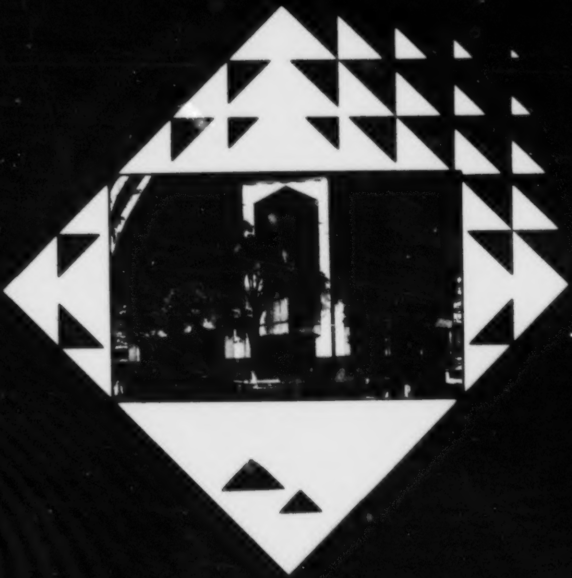
SCHEDULE OF DONATIONS

FOR THE YEAR ENDED MARCH 31, 1989

	$
Brought forward	170,076
UNRESTRICTED DONATIONS (cont'd)	
Non-designated (cont'd)	
In memory of Mary Frances M. Smith	510
Donation Standard Aero Employees	2,000
In memory of Marjorie Storey	540
In memory of John Thompson	500
Estate of Dr. H.W. Tweed	5,342
Donation Mr. O. Van De Wille	500
In memory of William Willis	2,200
Winnipeg Foundation -	
In memory of Samuel & Jessie Badham	2,250
George Gordon Fund	725
Harry Little Family Fund	1,400
Thomas William & Anna Ronald Lowe Memorial Fund	2,000
Lewis & Pearl C. Roth	5,718
Mr. & Mrs. Joseph Secter	1,610
Samuel & Sally Stern & son Ronald	1,002
Frank Topper & Emma Topper Memorial Fund	2,545
Joseph P. Wolinsky Fund	500
In memory of C. Maureen Younger	715
Other memorial contributions and donations in amounts of less than $500	69,885
	270,018
Designated	
Canadian Cancer Society	12,500
Donation - Kiwanis Club	6,319
In memory of S. Kofsky	3,105
Marnie McDiarmid Foundation	20,000
Donation Order of Eastern Star	1,000
Donation Pocklington Foundation	15,077
Estate Anne Portney	103,050
Gwen & Joseph Secter Fund	5,000
In memory of Anne Tate	4,000
Donation Hon. G. E. Tritschler	1,000
Donation Mr. A. Warkentin	1,500
Other donations in amounts of less than $500	1,720
	174,271
	444,289

Coopers
&Lybrand

1988 ANNUAL REPORT
STATISTICS



MANITOBA CANCER TREATMENT
AND RESEARCH FOUNDATION

CANCER INCIDENCE AND MORTALITY IN THE PROVINCE OF MANITOBA DURING THE CALENDAR YEAR 1988

The following self-explanatory Tables and Figures will illustrate the extent of morbidity and mortality from cancer. Unless otherwise indicated, Rates are based on Statistics Canada population estimates for 1988.

TABLE I

PLACE

DIAGNOSIS	**Male**	**Female**	**Total**
Health Sciences Centre	465	505	970
St. Boniface General Hospital	516	446	962
Other Hospitals in Greater Winnipeg	1,017	927	1,944
Other Hospitals in Manitoba	784	716	1,500
Hospitals Outside Manitoba	51	58	109
Doctors and Clinics	438	687	1,125
TOTAL	**3,271**	**3,339**	**6,610**

DEATH	***Male***	***Female***	***Total***
Hospitals-Greater Winnipeg	*741*	*595*	*1,336*
Hospitals-Outside Greater Winnipeg	*387*	*289*	*676*
Nursing Homes	*16*	*13*	*29*
Other-Greater Winnipeg	*73*	*75*	*148*
Other-Outside Greater Winnipeg	*66*	*55*	*121*
TOTAL	***1,283***	***1,027***	***2,310***

TABLE II

RESIDENCE

DIAGNOSIS	**Male**	**Female**	**Total**
Greater Winnipeg	1,723	1,944	3,667
Manitoba-Outside Greater Winnipeg	1,432	1,278	2,710
Non-Manitoba Residence	109	110	219
Residence Unknown	7	7	14
TOTAL	**3,271**	**3,339**	**6,610**

DEATH	***Male***	***Female***	***Total***
Greater Winnipeg	*808*	*669*	*1,477*
Manitoba-Outside Greater Winnipeg	*459*	*341*	*800*
Non-Manitoba Residence	*16*	*17*	*33*
Residence Unknown	*0*	*0*	*0*
TOTAL	***1,283***	***1,027***	***2,310***

TABLE IIa RESIDENTIAL DISTRIBUTION 1988

INCIDENCE

Residence	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Division 1	59	702.3	47	597.9	106	651.9
Division 2	88	430.1	85	426.9	173	428.5
Division 3	126	662.2	101	520.7	227	590.8
Division 4	44	753.4	47	835.5	91	793.7
Division 5	94	1,134.5	62	755.1	156	945.7
Division 6	36	642.8	36	645.7	72	644.2
Division 7	180	645.0	186	636.8	366	640.8
Division 8	57	841.3	40	620.1	97	733.4
Division 9	64	554.5	68	581.1	132	567.9
Division 10	13	339.4	12	342.3	25	340.8
Winnipeg	1,724	600.7	1,953	634.9	3,677	618.4
Division 12	41	504.3	41	530.0	82	516.8
Division 13	69	406.4	64	384.4	133	395.5
Division 14	35	455.7	32	454.8	67	455.3
Division 15	136	1,134.2	93	786.1	229	961.3
Division 16	39	722.2	36	695.6	75	709.2
Division 17	112	840.2	100	758.1	212	799.3
Division 18	97	861.0	69	642.4	166	754.3
Division 19	8	168.5	9	205.4	17	186.3
Division 20	52	832.6	52	865.2	104	848.6
Division 21	50	408.3	54	456.8	104	432.1
Division 22	24	152.5	27	182.2	51	166.9
Division 23	7	129.0	8	165.4	15	146.1
TOTAL	**3,155**	**602.3**	**3,222**	**597.5**	**6,377**	**599.9**

MORTALITY

Residence	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Division 1	*9*	*107.1*	*7*	*89.0*	*16*	*98.4*
Division 2	*29*	*141.7*	*18*	*90.4*	*47*	*116.4*
Division 3	*44*	*231.2*	*24*	*123.7*	*68*	*176.9*
Division 4	*20*	*342.4*	*12*	*213.3*	*32*	*279.1*
Division 5	*18*	*217.2*	*14*	*170.5*	*32*	*193.9*
Division 6	*8*	*142.8*	*13*	*233.1*	*21*	*187.9*
Division 7	*81*	*290.2*	*70*	*239.6*	*151*	*264.4*
Division 8	*10*	*147.6*	*6*	*93.0*	*16*	*120.9*
Division 9	*28*	*242.6*	*25*	*213.6*	*53*	*228.0*
Division 10	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Winnipeg	*808*	*281.5*	*669*	*217.4*	*1,477*	*248.4*
Division 12	*8*	*98.4*	*9*	*116.3*	*17*	*107.1*
Division 13	*22*	*129.6*	*17*	*102.1*	*39*	*116.0*
Division 14	*15*	*195.3*	*10*	*142.1*	*25*	*169.8*
Division 15	*38*	*316.9*	*37*	*312.7*	*75*	*314.8*
Division 16	*17*	*314.8*	*7*	*135.2*	*24*	*226.9*
Division 17	*43*	*322.5*	*30*	*227.4*	*73*	*275.2*
Division 18	*29*	*257.4*	*12*	*111.7*	*41*	*186.3*
Division 19	*1*	*21.0*	*0*	*0.0*	*1*	*10.9*
Division 20	*16*	*256.2*	*13*	*216.3*	*29*	*236.6*
Division 21	*15*	*122.4*	*9*	*76.1*	*24*	*99.7*
Division 22	*6*	*38.1*	*8*	*53.9*	*14*	*45.8*
Division 23	*2*	*36.8*	*0*	*0.0*	*2*	*19.4*
TOTAL	***1,267***	***241.9***	***1,010***	***187.3***	***2,277***	***214.2***

NOTE: Rates are based on Statistics Canada 1986 Census Data

STATISTICS CANADA

Standard Geographical Classification
Manitoba Census Divisions (1976)

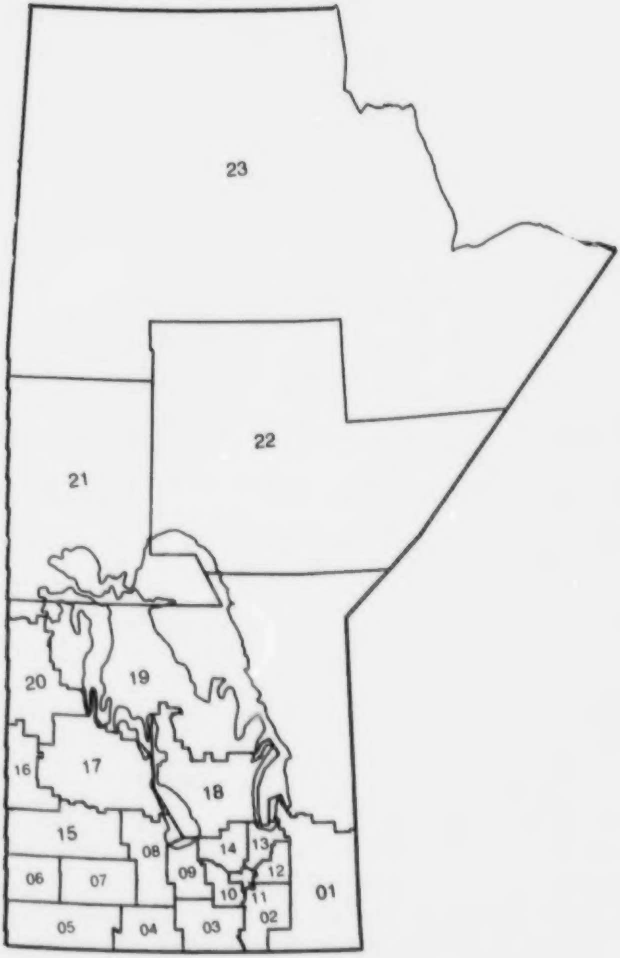

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TABLE III AGE and SEX DISTRIBUTION 1988

INCIDENCE

Age Group	Male	Rate	Female	Rate	TOTAL	RATE
0 - 4	8	18.8	13	32.1	21	25.3
5 - 9	5	12.4	4	10.4	9	11.4
10 - 14	5	12.4	2	5.2	7	8.9
15 - 19	9	21.1	11	27.2	20	24.0
20 - 24	14	31.3	55	125.5	69	77.9
25 - 29	31	63.5	125	260.9	156	161.3
30 - 34	41	89.9	133	294.9	174	191.8
35 - 39	43	107.7	128	316.8	171	212.9
40 - 44	64	184.9	132	385.9	196	284.8
45 - 49	94	350.7	131	486.9	225	418.9
50 - 54	146	616.0	156	658.2	302	637.1
55 - 59	253	1,076.5	207	855.3	460	964.3
60 - 64	367	1,616.7	329	1,305.5	696	1,453.0
65 - 69	532	2,633.6	390	1,585.3	922	2,058.0
70 - 74	544	3,378.8	440	2,167.4	984	2,703.2
75 - 79	478	4,156.5	401	2,490.6	879	3,184.7
80 - 84	293	4,373.1	260	2,385.3	553	3,142.0
85 - 89	157	4,906.2	204	3,457.6	361	3,967.0
90 and over	68	5,666.6	98	2,969.6	166	3,688.8
Unknown	3	0.0	3	0.0	6	0.0
TOTAL	**3,155**	**589.8**	**3,222**	**586.0**	**6,377**	**587.9**

MORTALITY

Age Group	*Male*	*Rate*	*Female*	*Rate*	*TOTAL*	*RATE*
0 - 4	*1*	*2.3*	*2*	*4.9*	*3*	*3.6*
5 - 9	*1*	*2.4*	*1*	*2.6*	*2*	*2.5*
10 - 14	*3*	*7.4*	*1*	*2.6*	*4*	*5.0*
15 - 19	*1*	*2.3*	*0*	*0.0*	*1*	*1.2*
20 - 24	*3*	*6.7*	*1*	*2.2*	*4*	*4.5*
25 - 29	*7*	*14.3*	*1*	*2.0*	*8*	*8.2*
30 - 34	*3*	*6.5*	*8*	*17.7*	*11*	*12.1*
35 - 39	*11*	*27.5*	*13*	*32.1*	*24*	*29.8*
40 - 44	*20*	*57.8*	*18*	*52.6*	*38*	*55.2*
45 - 49	*27*	*100.7*	*27*	*100.3*	*54*	*100.5*
50 - 54	*55*	*232.0*	*55*	*232.0*	*110*	*232.0*
55 - 59	*86*	*365.9*	*72*	*297.5*	*158*	*331.2*
60 - 64	*155*	*682.8*	*109*	*432.5*	*264*	*551.1*
65 - 69	*181*	*896.0*	*127*	*516.2*	*308*	*687.5*
70 - 74	*226*	*1,403.7*	*158*	*778.3*	*384*	*1,054.9*
75 - 79	*198*	*1,721.7*	*155*	*962.7*	*353*	*1,278.9*
80 - 84	*144*	*2,149.2*	*118*	*1,082.5*	*262*	*1,488.6*
85 - 89	*95*	*2,968.7*	*89*	*1,508.4*	*184*	*2,021.9*
90 and over	*50*	*4,166.6*	*55*	*1,666.6*	*105*	*2,333.3*
Unknown	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***1,267***	***236.8***	***1,010***	***183.7***	***2,277***	***209.9***

INCIDENCE
AND
MORTALITY

INCIDENCE & MORTALITY 1988

Digestive System

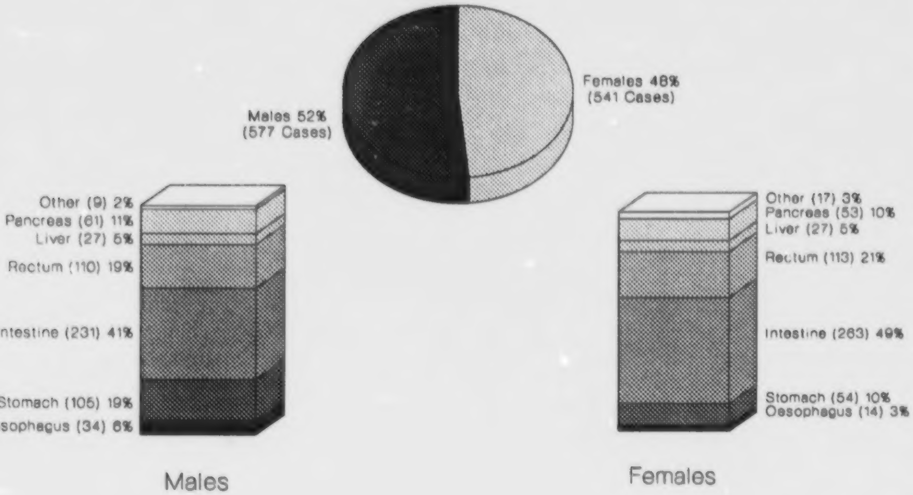
TABLE IV **DIGESTIVE SYSTEM 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	2	0.7	4	1.6	6	1.1
30-39	6	7.0	5	5.8	11	6.4
40-49	18	29.3	23	37.6	41	33.4
50-59	72	152.5	55	114.8	127	133.5
60-69	183	426.5	131	263.0	314	338.7
70-79	176	637.6	173	475.2	348	543.7
80-89	99	1,000.0	125	744.0	223	835.2
90 and over	20	1,666.6	24	727.2	44	977.7
Age not stated	1	0.0	1	0.0	2	0.0
TOTAL	**577**	**107.8**	**541**	**98.3**	**1,118**	**103.0**

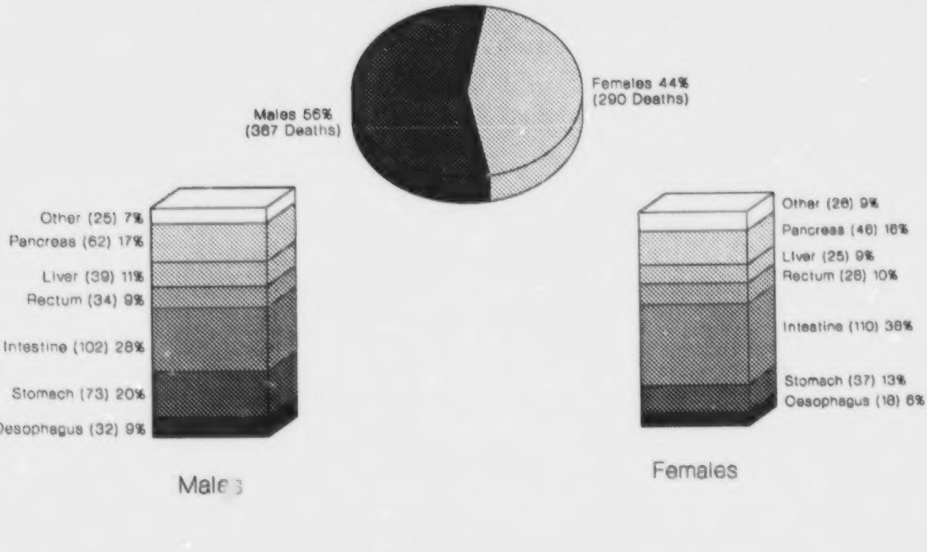
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*1*	*0.3*	*1*	*0.4*	*2*	*0.3*
30-39	*2*	*2.3*	*5*	*5.8*	*7*	*4.0*
40-49	*11*	*17.9*	*7*	*11.4*	*18*	*14.6*
50-59	*49*	*103.8*	*22*	*45.9*	*71*	*74.6*
60-69	*97*	*226.1*	*57*	*114.4*	*154*	*166.1*
70-79	*118*	*427.5*	*95*	*260.9*	*213*	*332.8*
80-89	*71*	*717.1*	*83*	*494.0*	*154*	*576.7*
90 and over	*18*	*1,500.0*	*20*	*606.0*	*38*	*844.4*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***367***	***68.6***	***290***	***52.7***	***657***	***60.5***

Digestive System 1988

Incidence



Mortality



Digestive System (Cont.)

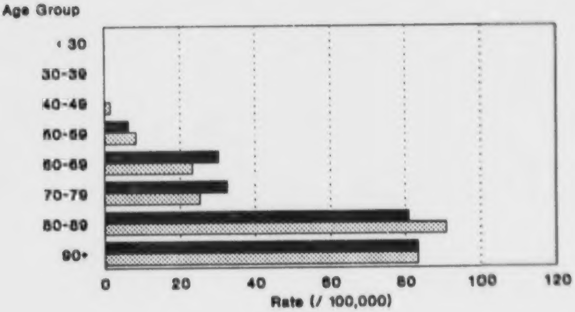
TABLE IVa **OESOPHAGUS 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	0	0.0	0	0.0	0	0.0
30-39	0	0.0	0	0.0	0	0.0
40-49	0	0.0	0	0.0	0	0.0
50-59	3	6.3	1	2.0	4	4.2
60-69	13	30.3	3	6.0	16	17.2
70-79	9	32.6	4	10.9	13	20.3
80-89	8	80.8	4	23.8	12	44.9
90 and over	1	83.3	2	60.6	3	66.6
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**34**	**6.3**	**14**	**2.5**	**48**	**4.4**

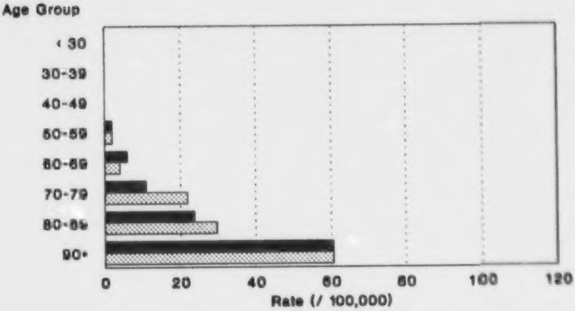
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*1*	*1.6*	*0*	*0.0*	*1*	*0.8*
50-59	*4*	*8.4*	*1*	*2.0*	*5*	*5.2*
60-69	*10*	*23.3*	*2*	*4.0*	*12*	*12.9*
70-79	*7*	*25.3*	*8*	*21.9*	*15*	*23.4*
80-89	*9*	*90.9*	*5*	*29.7*	*14*	*52.4*
90 and over	*1*	*83.3*	*2*	*60.6*	*3*	*66.6*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***32***	***5.9***	***18***	***3.2***	***50***	***4.6***

INCIDENCE & MORTALITY 1988
Oesophagus

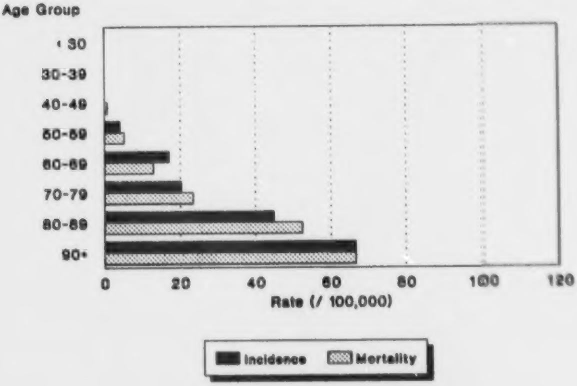
Males



Females



Total Population



Digestive System (Cont.)

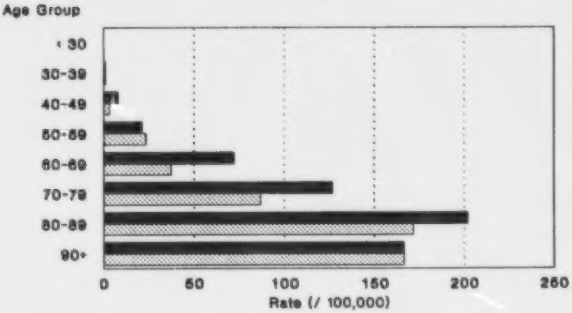
TABLE IVb **STOMACH 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	0	0.0	0	0.0	0	0.0
30-39	1	1.1	1	1.1	2	1.1
40-49	5	8.1	2	3.2	7	5.7
50-59	10	21.1	7	14.6	17	17.8
60-69	31	72.2	10	20.0	41	44.2
70-79	35	126.8	20	54.9	55	85.9
80-89	20	202.0	11	65.4	31	116.1
90 and over	2	166.6	3	90.9	5	111.1
Age not stated	1	0.0	0	0.0	1	0.0
TOTAL	**105**	**19.6**	**54**	**9.8**	**159**	**14.6**

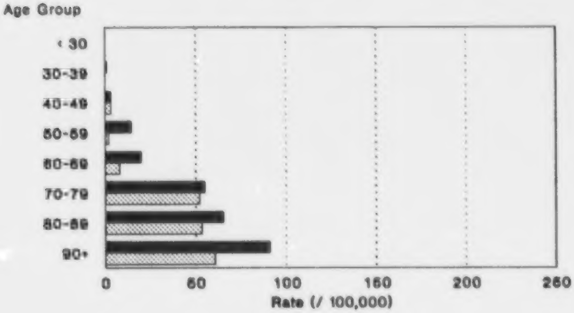
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*1*	*1.1*	*0*	*0.0*	*1*	*0.5*
40-49	*2*	*3.2*	*2*	*3.2*	*4*	*3.2*
50-59	*11*	*23.3*	*1*	*2.0*	*12*	*12.6*
60-69	*16*	*37.2*	*4*	*8.0*	*20*	*21.5*
70-79	*24*	*86.9*	*19*	*52.1*	*43*	*67.1*
80-89	*17*	*171.7*	*9*	*53.5*	*26*	*97.3*
90 and over	*2*	*166.6*	*2*	*60.6*	*4*	*88.8*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***73***	***13.6***	***37***	***6.7***	***110***	***10.1***

INCIDENCE & MORTALITY 1988
Stomach

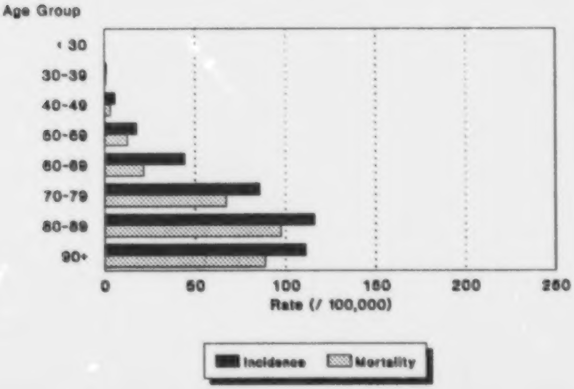
Males



Females



Total Population



Digestive System (Cont.)

TABLE IVc **LARGE BOWEL 1988**

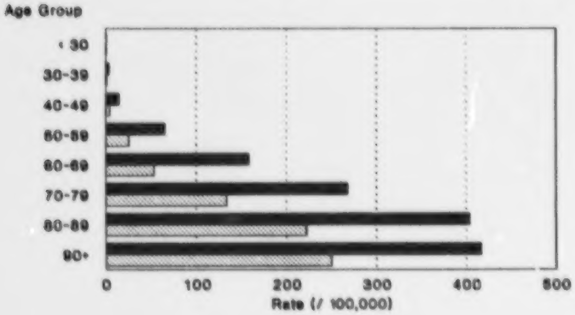
INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	1	0.3	3	1.2	4	0.7
30-39	3	3.5	1	1.1	4	2.3
40-49	9	14.6	12	19.6	21	17.1
50-59	31	65.6	21	43.8	52	54.6
60-69	68	158.5	74	148.5	142	153.1
70-79	74	268.1	73	200.5	147	229.6
80-89	40	404.0	65	386.9	105	393.2
90 and over	5	416.6	13	393.9	18	400.0
Age not stated	0	0.0	1	0.0	1	0.0
TOTAL	**231**	**43.1**	**263**	**47.8**	**494**	**45.5**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	**TOTAL**	***RATE***
Under 30	*1*	*0.3*	*0*	*0.0*	*1*	*0.1*
30-39	*1*	*1.1*	*2*	*2.3*	*3*	*1.7*
40-49	*3*	*4.8*	*1*	*1.6*	*4*	*3.2*
50-59	*12*	*25.4*	*7*	*14.6*	*19*	*19.9*
60-69	*23*	*53.6*	*28*	*56.2*	*51*	*55.0*
70-79	*37*	*134.0*	*32*	*87.9*	*69*	*107.8*
80-89	*22*	*222.2*	*32*	*190.4*	*54*	*202.2*
90 and over	*3*	*250.0*	*8*	*242.4*	*11*	*244.4*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***102***	***19.0***	***110***	***20.0***	***212***	***19.5***

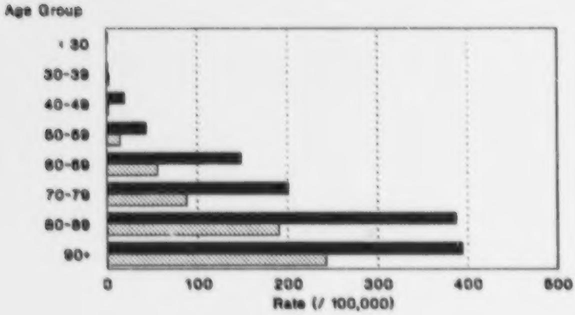
INCIDENCE & MORTALITY 1988

Large Bowel

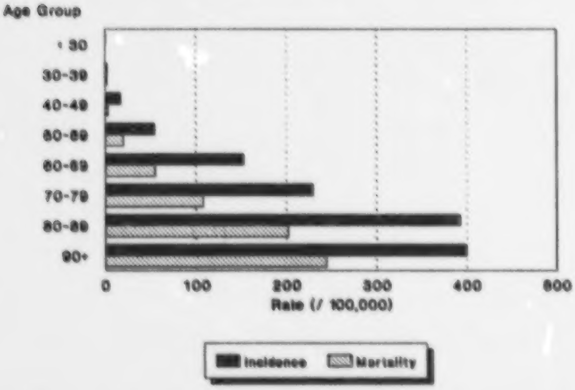
Males



Females



Total Population



Digestive System (Cont.)

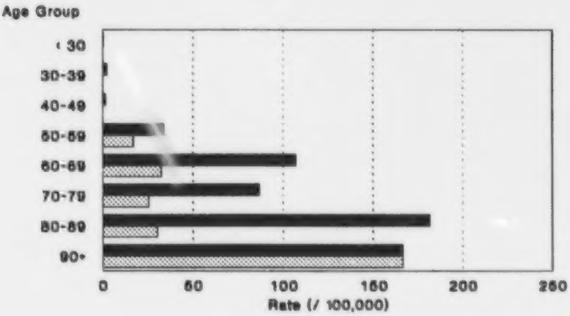
TABLE IVd RECTUM and RECTOSIGMOID JUNCTION 1988

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	1	0.3	0	0.0	1	0.1
30-39	2	2.3	2	2.3	4	2.3
40-49	1	1.6	4	6.5	5	4.0
50-59	16	33.8	17	35.4	33	34.7
60-69	46	107.2	19	38.1	65	70.1
70-79	24	86.9	46	126.3	70	109.3
80-89	18	181.8	19	113.0	37	138.5
90 and over	2	166.6	6	181.8	8	177.7
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**110**	**20.5**	**113**	**20.5**	**223**	**20.5**

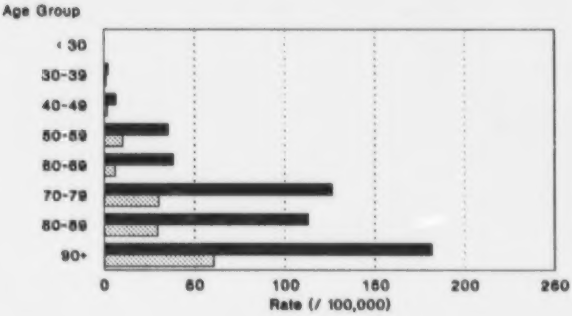
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*1*	*1.1*	*1*	*0.5*
40-49	*0*	*0.0*	*1*	*1.6*	*1*	*0.8*
50-59	*8*	*16.9*	*5*	*10.4*	*13*	*13.6*
60-69	*14*	*32.6*	*3*	*6.0*	*17*	*18.3*
70-79	*7*	*25.3*	*11*	*30.2*	*18*	*28.1*
80-89	*3*	*30.3*	*5*	*29.7*	*8*	*29.9*
90 and over	*2*	*166.6*	*2*	*60.6*	*4*	*88.8*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***34***	***6.3***	***28***	***5.0***	***62***	***5.7***

INCIDENCE & MORTALITY 1988
Rectum

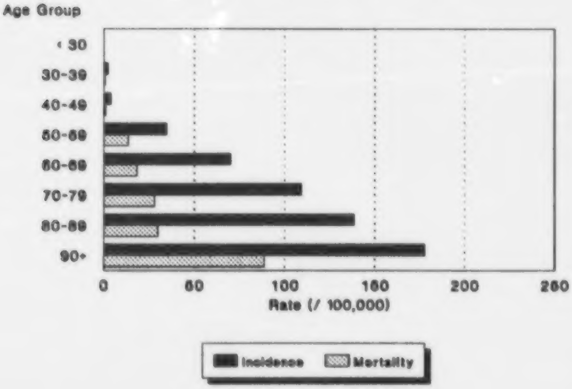
Males



Females



Total Population



Digestive System (Cont.)

TABLE IVe **LIVER and BILIARY PASSAGES[*] 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	0	0.0	1	0.4	1	0.1
30-39	0	0.0	0	0.0	0	0.0
40-49	2	3.2	1	1.6	3	2.4
50-59	4	8.4	2	4.1	6	6.3
60-69	4	9.3	8	16.0	12	12.9
70-79	9	32.6	11	30.2	20	31.2
80-89	5	50.5	4	23.8	9	33.7
90 and over	3	250.0	0	0.0	3	66.6
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**27**	**5.0**	**27**	**4.9**	**54**	**4.9**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*1*	*0.4*	*1*	*0.1*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*3*	*4.8*	*1*	*1.6*	*4*	*3.2*
50-59	*5*	*10.5*	*2*	*4.1*	*7*	*7.3*
60-69	*10*	*23.3*	*4*	*8.0*	*14*	*15.1*
70-79	*12*	*43.4*	*7*	*19.2*	*19*	*29.6*
80-89	*8*	*80.8*	*10*	*59.5*	*18*	*67.4*
90 and over	*1*	*83.3*	*0*	*0.0*	*1*	*22.2*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***39***	***7.2***	***25***	***4.5***	***64***	***5.9***

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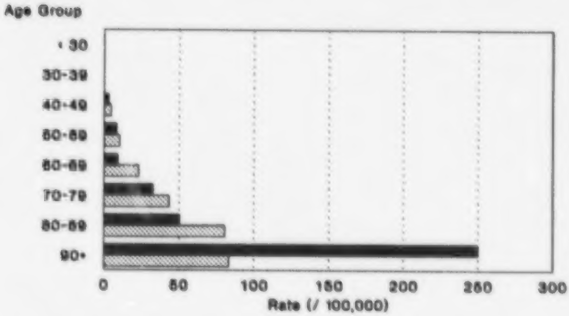
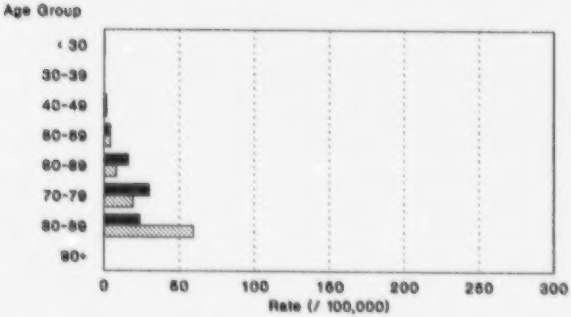
[*] This probably includes a number of cases of secondary metastatic disease - not defined in the death certificate.

INCIDENCE & MORTALITY 1988
Liver

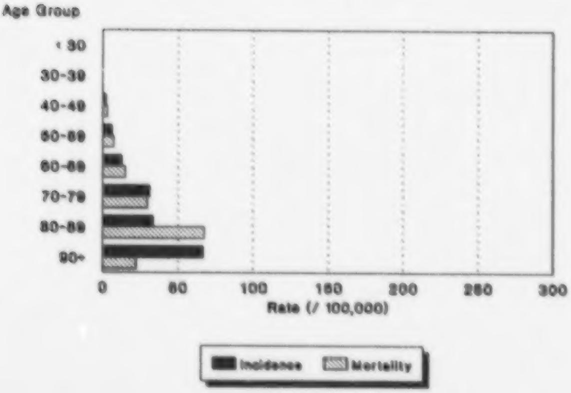
Males



Females



Total Population



Digestive System (Cont.)

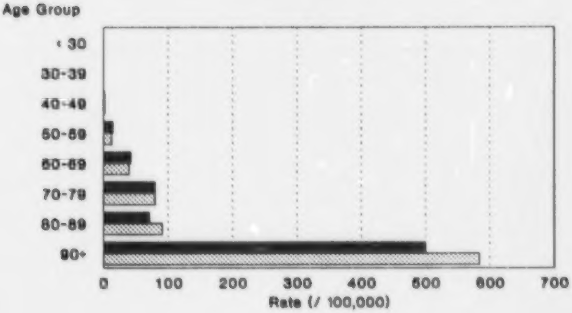
TABLE IVf **PANCREAS 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	0	0.0	0	0.0	0	0.0
30-39	0	0.0	0	0.0	0	0.0
40-49	1	1.6	1	1.6	2	1.6
50-59	7	14.8	5	10.4	12	12.6
60-69	18	41.9	12	24.0	30	32.3
70-79	22	79.7	17	46.7	39	60.9
80-89	7	70.7	17	101.1	24	89.8
90 and over	6	500.0	1	30.3	7	155.5
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	61	11.4	53	9.6	114	10.5

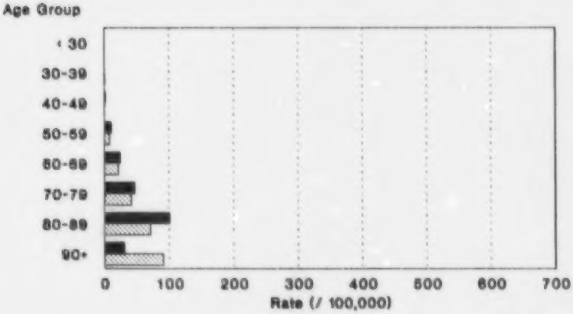
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*1*	*1.1*	*1*	*0.5*
40-49	*1*	*1.6*	*0*	*0.0*	*1*	*0.8*
50-59	*6*	*12.7*	*4*	*8.3*	*10*	*10.5*
60-69	*17*	*39.6*	*11*	*22.0*	*28*	*30.2*
70-79	*22*	*79.7*	*15*	*41.2*	*37*	*57.8*
80-89	*9*	*90.9*	*12*	*71.4*	*21*	*78.6*
90 and over	*7*	*583.3*	*3*	*90.9*	*10*	*222.2*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***62***	***11.5***	***46***	***8.3***	***108***	***9.9***

INCIDENCE & MORTALITY 1988
Pancreas

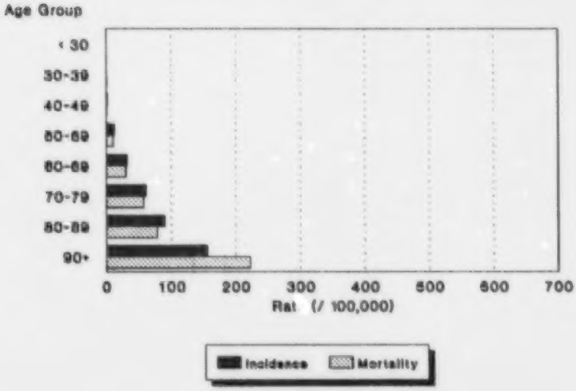
Males



Females



Total Population



INCIDENCE & MORTALITY 1988

Buccal Cavity & Pharynx

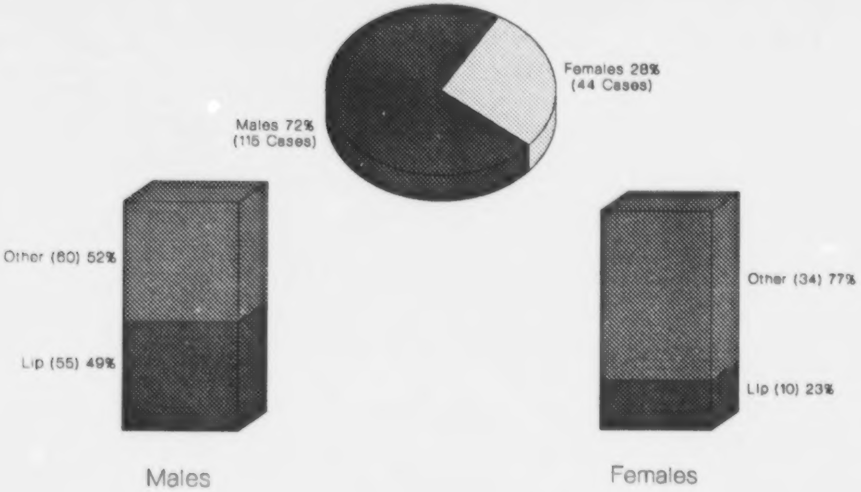
TABLE V **BUCCAL CAVITY AND PHARYNX 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	2	0.7	0	0.0	2	0.3
30-39	3	3.5	1	1.1	4	2.3
40-49	11	17.9	1	1.6	12	9.7
50-59	23	48.7	2	4.1	25	26.2
60-69	39	90.9	12	24.0	51	55.0
70-79	24	86.9	14	38.4	38	59.3
80-89	12	121.2	12	71.4	24	89.8
90 and over	1	83.3	2	60.6	3	66.6
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**115**	**21.4**	**44**	**8.0**	**159**	**14.6**

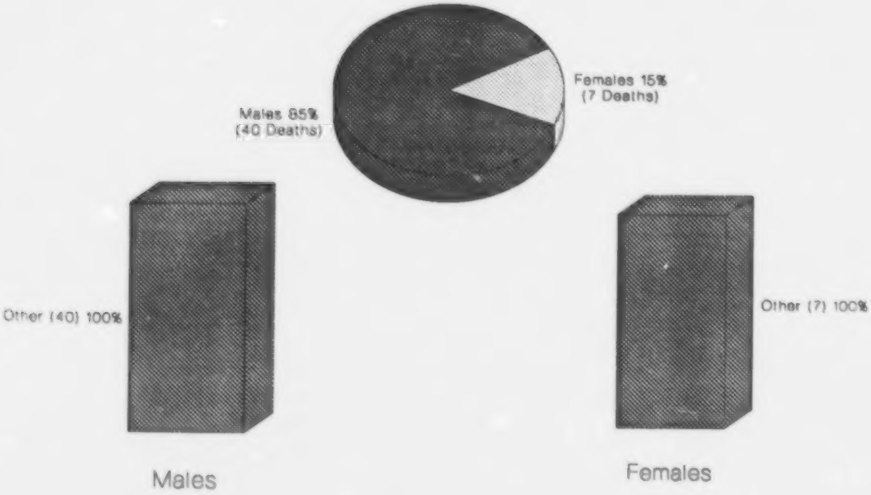
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*1*	*1.1*	*0*	*0.0*	*1*	*0.5*
40-49	*1*	*1.6*	*0*	*0.0*	*1*	*0.8*
50-59	*9*	*19.0*	*1*	*2.0*	*10*	*10.5*
60-69	*16*	*37.2*	*1*	*2.0*	*17*	*18.3*
70-79	*7*	*25.3*	*2*	*5.4*	*9*	*14.0*
80-89	*6*	*60.6*	*3*	*17.8*	*9*	*33.7*
90 and over	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***40***	***7.4***	***7***	***1.2***	***47***	***4.3***

Buccal Cavity & Pharynx 1988

Incidence



Mortality



Buccal Cavity & Pharynx (Cont.)

TABLE Va **LIP 1988**

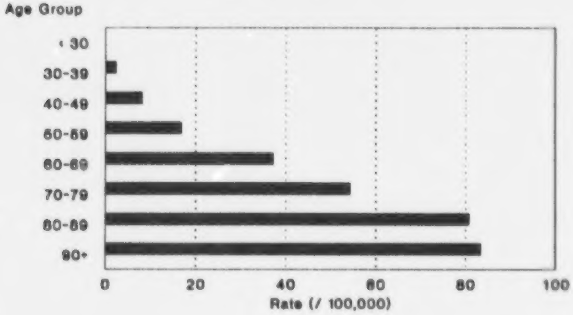
INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	0	0.0	0	0.0	0	0.0
30-39	2	2.3	0	0.0	2	1.1
40-49	5	8.1	0	0.0	5	4.0
50-59	8	16.9	0	0.0	8	8.4
60-69	16	37.2	0	0.0	16	17.2
70-79	15	54.3	5	13.7	20	31.2
80-89	8	80.8	4	23.8	12	44.9
90 and over	1	83.3	1	30.3	2	44.4
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**55**	**10.2**	**10**	**1.8**	**65**	**5.9**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
50-59	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
60-69	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
70-79	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
80-89	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
90 and over	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***0***	***0.0***	***0***	***0.0***	***0***	***0.0***

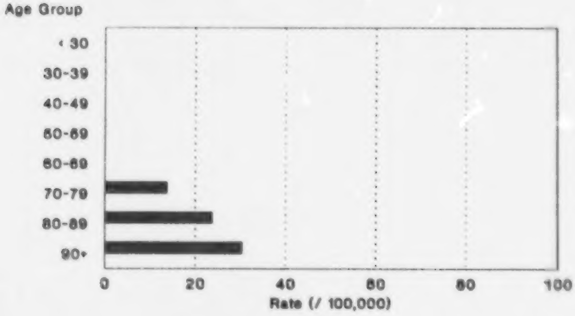
INCIDENCE & MORTALITY 1988

Lip

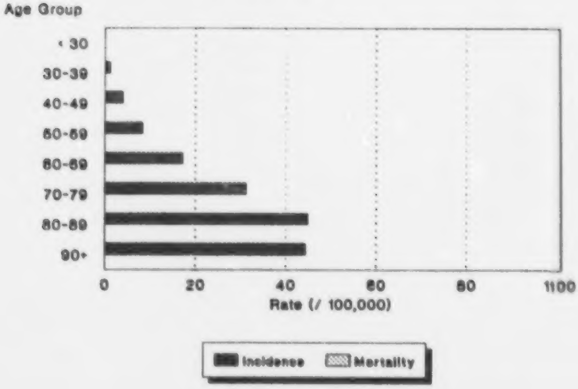
Males



Females



Total Population



INCIDENCE & MORTALITY 1988

Respiratory System

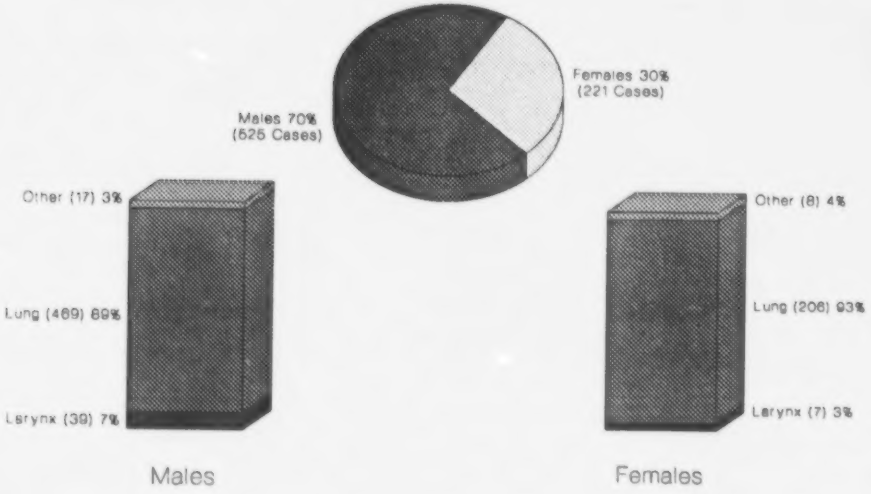
TABLE VI **RESPIRATORY SYSTEM 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	3	1.1	0	0.0	3	0.5
30-39	5	5.8	4	4.6	9	5.2
40-49	17	27.6	17	27.8	34	27.7
50-59	83	175.8	41	85.5	124	130.3
60-69	166	386.9	70	140.5	236	254.5
70-79	183	663.0	68	186.8	251	392.1
80-89	65	656.5	15	89.2	80	299.6
90 and over	3	250.0	6	181.8	9	200.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**525**	**98.1**	**221**	**40.1**	**746**	**68.7**

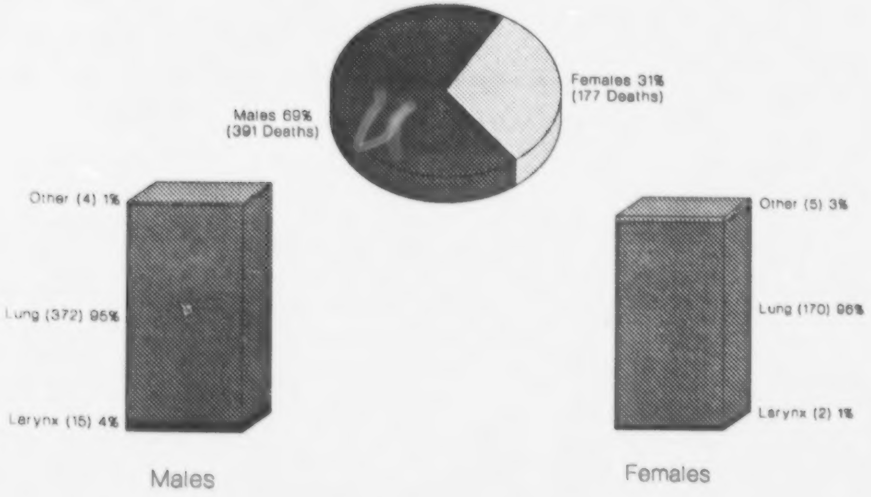
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*2*	*0.7*	*0*	*0.0*	*2*	*0.3*
30-39	*1*	*1.1*	*1*	*1.1*	*2*	*1.1*
40-49	*13*	*21.1*	*8*	*13.0*	*21*	*17.1*
50-59	*45*	*95.3*	*27*	*56.3*	*72*	*75.7*
60-69	*125*	*291.3*	*56*	*112.4*	*181*	*195.2*
70-79	*135*	*489.1*	*59*	*162.0*	*194*	*303.1*
80-89	*65*	*656.5*	*21*	*125.0*	*86*	*322.0*
90 and over	*5*	*416.6*	*5*	*151.5*	*10*	*222.2*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***391***	***73.0***	***177***	***32.1***	***568***	***52.3***

Respiratory System 1988

Incidence



Mortality



Respiratory System (Cont.)

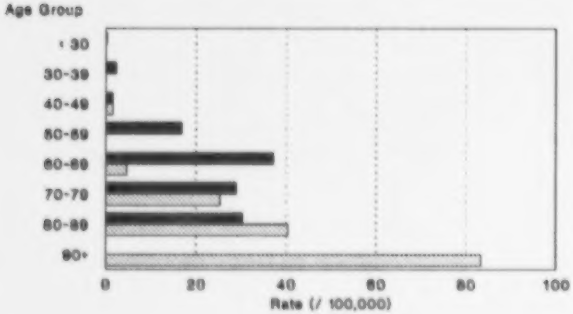
TABLE VIa **LARYNX 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	1	0.3	0	0.0	1	0.1
30-39	2	2.3	0	0.0	2	1.1
40-49	1	1.6	1	1.6	2	1.6
50-59	8	16.9	3	6.2	11	11.5
60-69	16	37.2	1	2.0	17	18.3
70-79	8	28.9	1	2.7	9	14.0
80-89	3	30.3	1	5.9	4	14.9
90 and over	0	0.0	0	0.0	0	0.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**39**	**7.2**	**7**	**1.2**	**46**	**4.2**

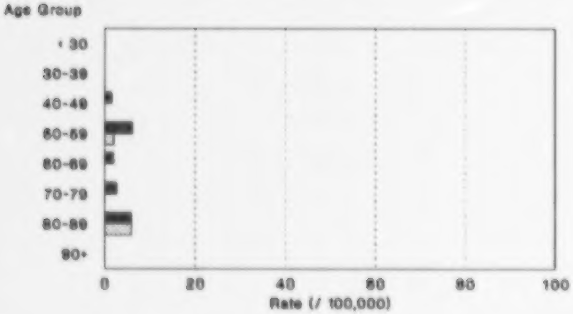
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*1*	*1.6*	*0*	*0.0*	*1*	*0.8*
50-59	*0*	*0.0*	*1*	*2.0*	*1*	*1.0*
60-69	*2*	*4.6*	*0*	*0.0*	*2*	*2.1*
70-79	*7*	*25.3*	*0*	*0.0*	*7*	*10.9*
80-89	*4*	*40.4*	*1*	*5.9*	*5*	*18.7*
90 and over	*1*	*83.3*	*0*	*0.0*	*1*	*22.2*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***15***	***2.8***	***2***	***0.3***	***17***	***1.5***

INCIDENCE & MORTALITY 1988
Larynx

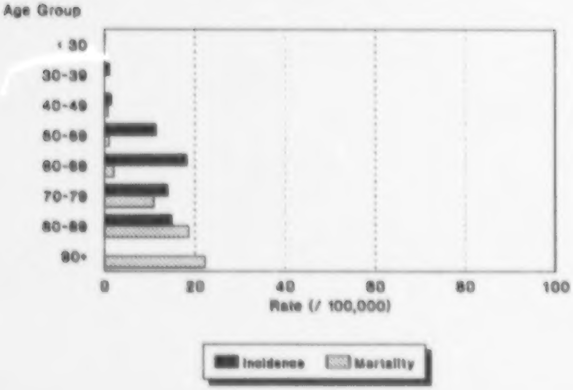
Males



Females



Total Population



Respiratory System (Cont.)

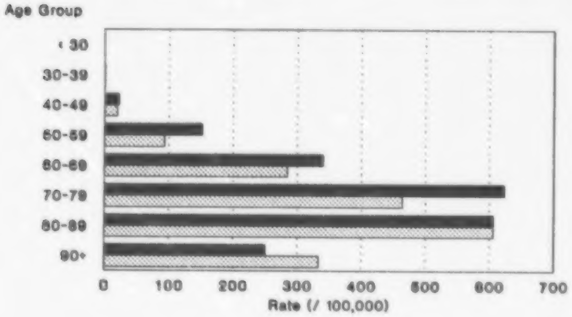
TABLE VIb **TRACHEA, BRONCHUS and LUNG 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	1	0.3	0	0.0	1	0.1
30-39	1	1.1	1	1.1	2	1.1
40-49	14	22.8	16	26.1	30	24.4
50-59	72	152.5	38	79.3	110	115.6
60-69	146	340.3	67	134.5	213	229.7
70-79	172	623.1	65	178.5	237	370.3
80-89	60	606.0	13	77.3	73	273.4
90 and over	3	250.0	6	181.8	9	200.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**469**	**87.6**	**206**	**37.4**	**675**	**62.2**

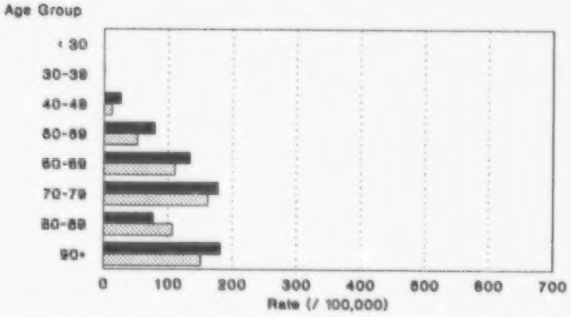
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*1*	*0.3*	*0*	*0.0*	*1*	*0.1*
30-39	*1*	*1.1*	*0*	*0.0*	*1*	*0.5*
40-49	*12*	*19.5*	*8*	*13.0*	*20*	*16.3*
50-59	*44*	*93.2*	*25*	*52.1*	*69*	*72.5*
60-69	*122*	*284.3*	*55*	*110.4*	*177*	*190.9*
70-79	*128*	*463.7*	*59*	*162.0*	*187*	*292.1*
80-89	*60*	*606.0*	*18*	*107.1*	*78*	*292.1*
90 and over	*4*	*333.3*	*5*	*151.5*	*9*	*200.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***372***	***69.5***	***170***	***30.9***	***542***	***49.9***

INCIDENCE & MORTALITY 1988
Trachea, Bronchus & Lung

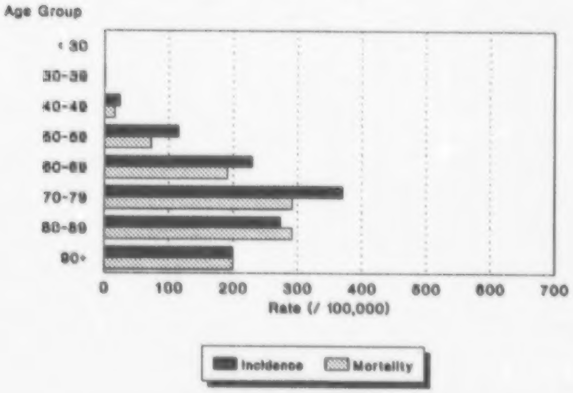
Males



Females



Total Population



INCIDENCE & MORTALITY 1988

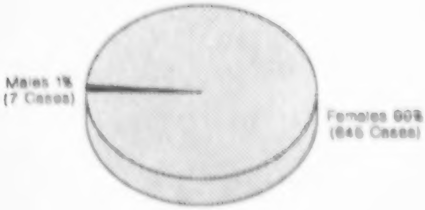
Breast

TABLE VII **BREAST 1988**

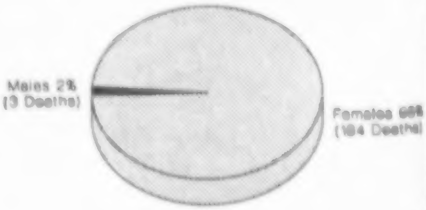
INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	0	0.0	4	1.6	4	0.7
30-39	0	0.0	26	30.4	26	15.2
40-49	0	0.0	84	137.5	84	68.6
50-59	1	2.1	117	244.3	118	124.1
60-69	4	9.3	150	301.2	154	166.1
70-79	1	3.6	168	461.5	169	264.0
80-89	1	10.1	86	511.9	87	325.8
90 and over	0	0.0	10	303.0	10	222.2
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**7**	**1.3**	**645**	**117.3**	**652**	**60.1**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*4*	*4.6*	*4*	*2.3*
40-49	*0*	*0.0*	*12*	*19.6*	*12*	*9.7*
50-59	*0*	*0.0*	*36*	*75.1*	*36*	*37.8*
60-69	*1*	*2.3*	*43*	*86.3*	*44*	*47.4*
70-79	*1*	*3.6*	*49*	*134.6*	*50*	*78.1*
80-89	*1*	*10.1*	*28*	*166.6*	*29*	*108.6*
90 and over	*0*	*0.0*	*12*	*363.6*	*12*	*266.6*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	**3**	**0.5**	**184**	**33.4**	**187**	**17.2**

Incidence



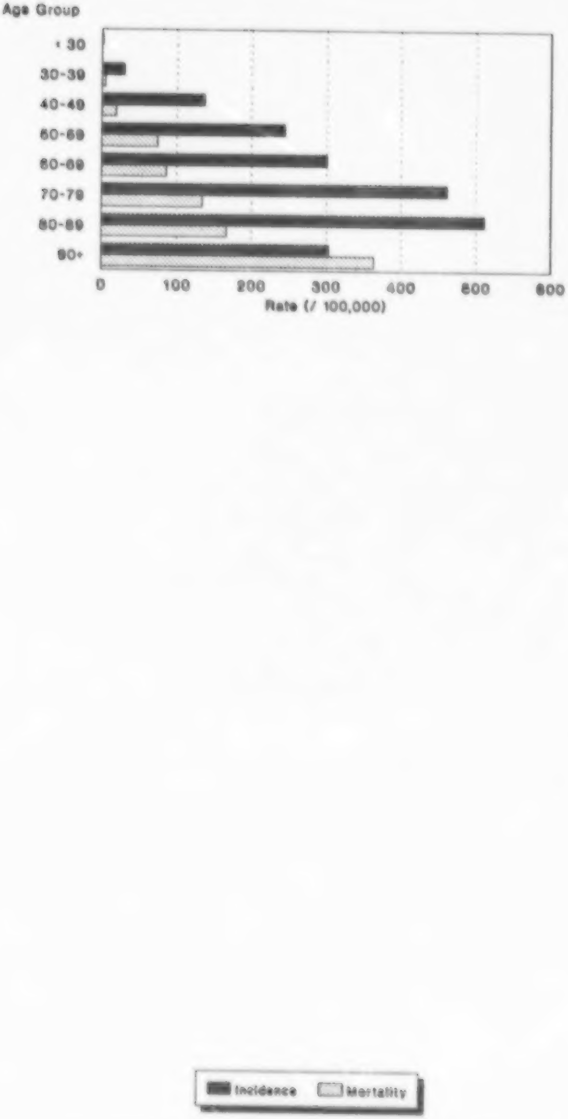
Mortality



INCIDENCE & MORTALITY 1988

Breast

Females



INCIDENCE & MORTALITY 1988

Urinary Tract

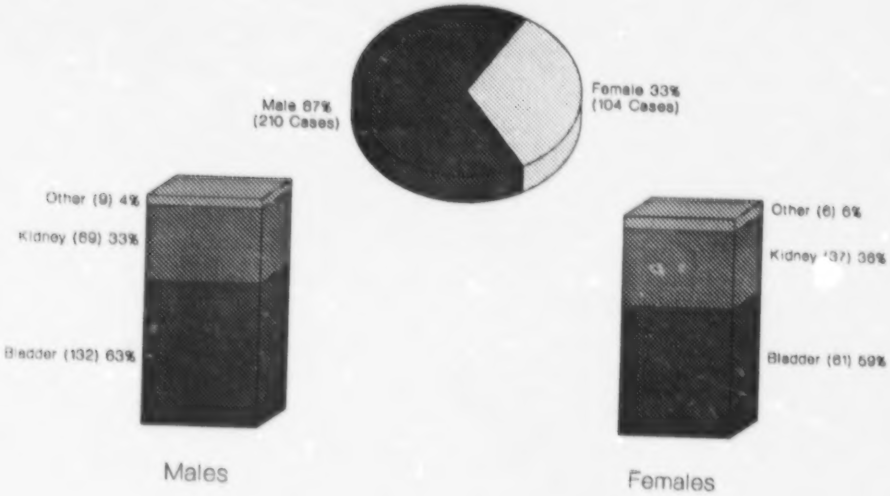
TABLE VIII **URINARY TRACT 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	2	0.7	1	0.4	3	0.5
30-39	4	4.6	0	0.0	4	2.3
40-49	10	16.2	8	13.0	18	14.6
50-59	24	50.8	8	16.7	32	33.6
60-69	84	195.8	20	40.1	104	112.1
70-79	57	206.5	43	118.1	100	156.2
80-89	26	262.6	19	113.0	45	168.5
90 and over	3	250.0	5	151.5	8	177.7
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**210**	**39.2**	**104**	**18.9**	**314**	**28.9**

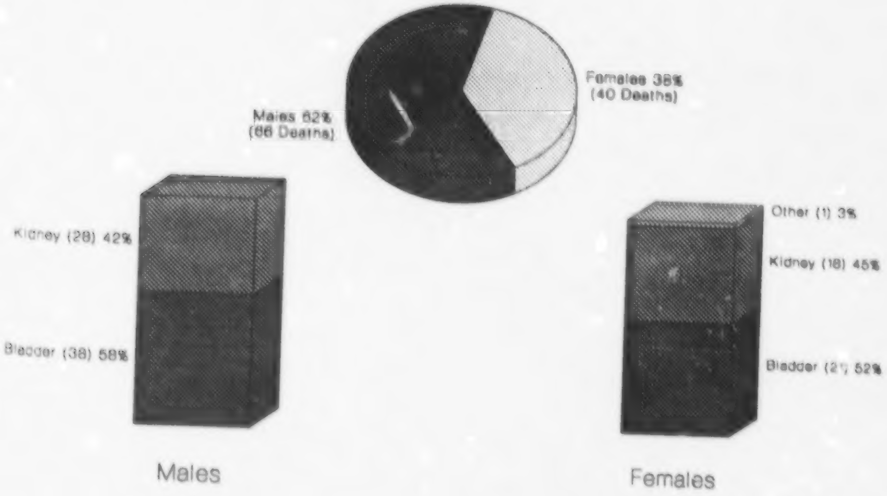
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*3*	*4.8*	*1*	*1.6*	*4*	*3.2*
50-59	*8*	*16.9*	*4*	*8.3*	*12*	*12.6*
60-69	*16*	*37.2*	*7*	*14.0*	*23*	*24.8*
70-79	*25*	*90.5*	*13*	*35.7*	*38*	*59.3*
80-89	*11*	*111.1*	*11*	*65.4*	*22*	*82.3*
90 and over	*3*	*250.0*	*4*	*121.2*	*7*	*155.5*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***66***	***12.3***	***40***	***7.2***	***106***	***9.7***

Urinary Tract 1988

Incidence



Mortality



Urinary Tract (Cont.)

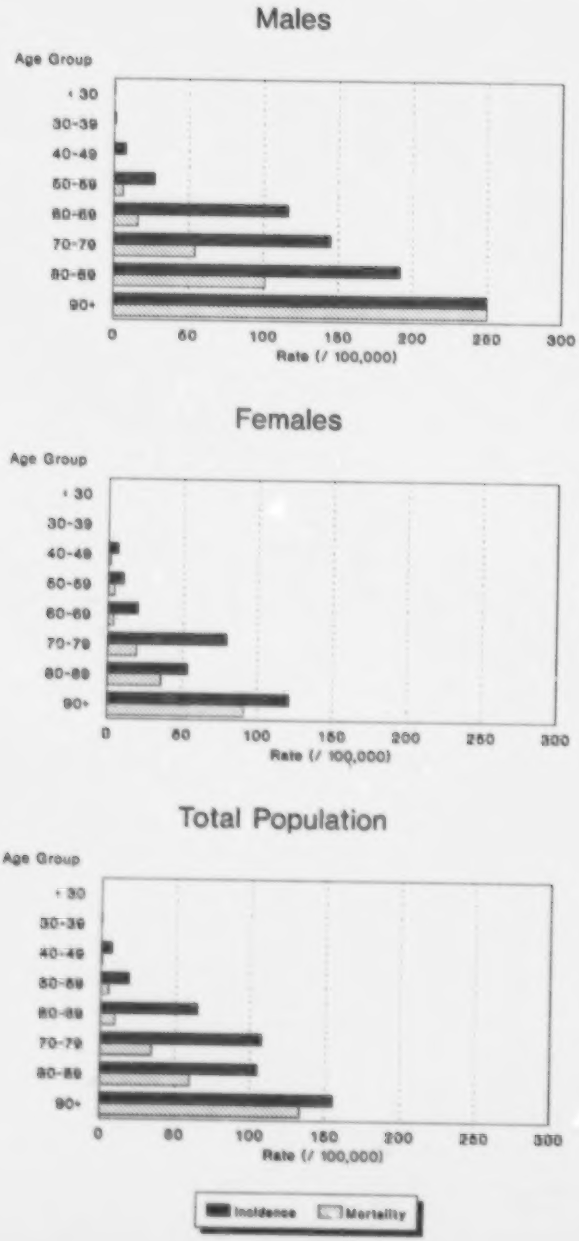
TABLE VIIIa **BLADDER 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	1	0.3	0	0.0	1	0.1
30-39	1	1.1	0	0.0	1	0.5
40-49	5	8.1	4	6.5	9	7.3
50-59	13	27.5	5	10.4	18	18.9
60-69	50	116.5	10	20.0	60	64.7
70-79	40	144.9	29	79.6	69	107.8
80-89	19	191.9	9	53.5	28	104.8
90 and over	3	250.0	4	121.2	7	155.5
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**132**	**24.6**	**61**	**11.0**	**193**	**17.7**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*0*	*0.0*	*1*	*1.6*	*1*	*0.8*
50-59	*3*	*6.3*	*2*	*4.1*	*5*	*5.2*
60-69	*7*	*16.3*	*2*	*4.0*	*9*	*9.7*
70-79	*15*	*54.3*	*7*	*19.2*	*22*	*34.3*
80-89	*10*	*101.0*	*6*	*35.7*	*16*	*59.9*
90 and over	*3*	*250.0*	*3*	*90.9*	*6*	*133.3*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Total	***38***	***7.1***	***21***	***3.8***	***59***	***5.4***

INCIDENCE & MORTALITY 1988

Bladder



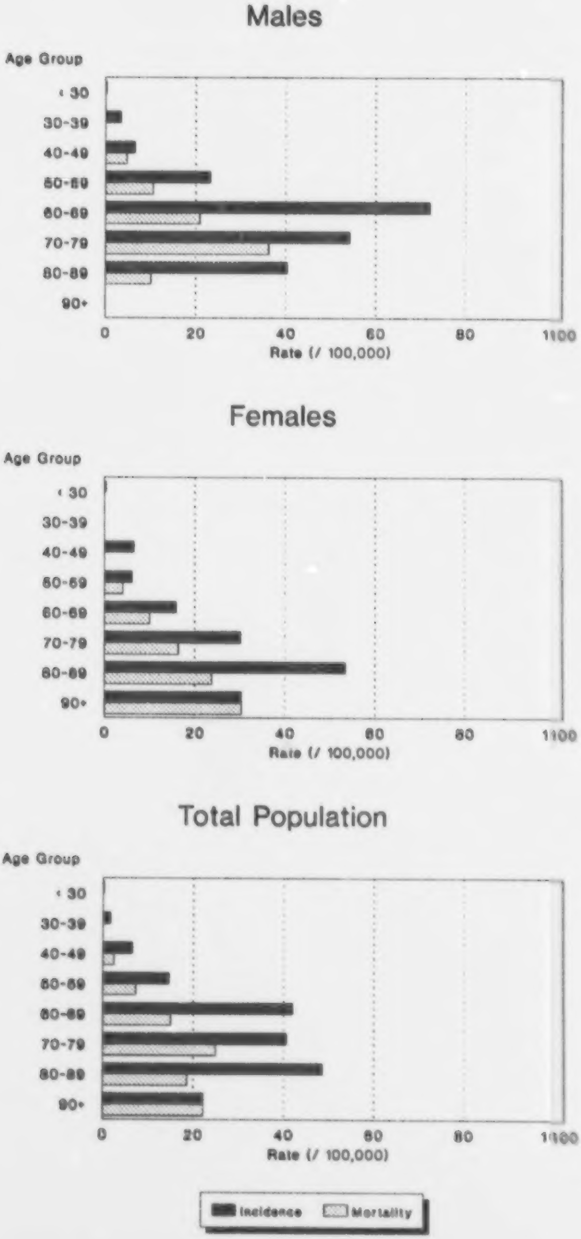
Urinary Tract (Cont.)

TABLE VIIIb **KIDNEY 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	1	0.3	1	0.4	2	0.3
30-39	3	3.5	0	0.0	3	1.7
40-49	4	6.5	4	6.5	8	6.5
50-59	11	23.3	3	6.2	14	14.7
60-69	31	72.2	8	16.0	39	42.0
70-79	15	54.3	11	30.2	26	40.6
80-89	4	40.4	9	53.5	13	48.6
90 and over	0	0.0	1	30.3	1	22.2
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**69**	**12.8**	**37**	**6.7**	**106**	**9.7**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*3*	*4.8*	*0*	*0.0*	*3*	*2.4*
50-59	*5*	*10.5*	*2*	*4.1*	*7*	*7.3*
60-69	*9*	*20.9*	*5*	*10.0*	*14*	*15.1*
70-79	*10*	*36.2*	*6*	*16.4*	*16*	*25.0*
80-89	*1*	*10.1*	*4*	*23.8*	*5*	*18.7*
90 and over	*0*	*0.0*	*1*	*30.3*	*1*	*22.2*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***28***	***5.2***	***18***	***3.2***	***46***	***4.2***

INCIDENCE & MORTALITY 1988
Kidney



Males

Females

Total Population

INCIDENCE & MORTALITY 1988

Skin

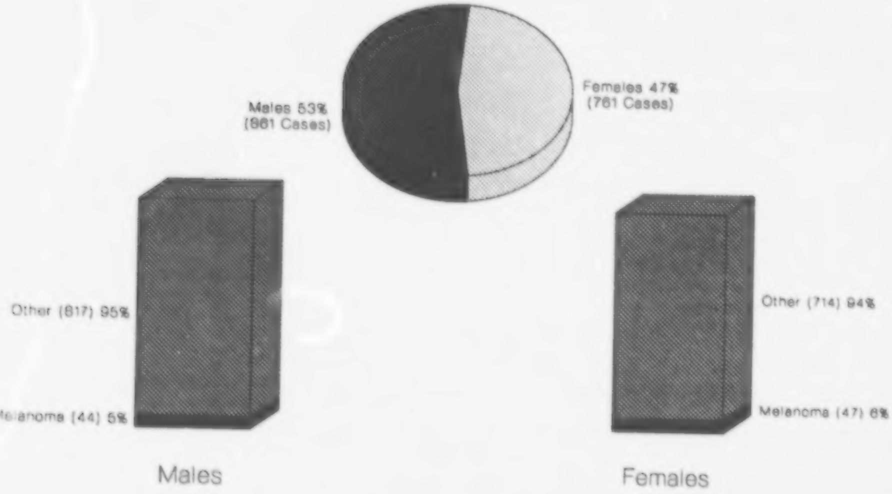
TABLE IX **SKIN 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	14	5.4	21	8.4	35	6.8
30-39	29	33.9	46	53.8	75	43.8
40-49	59	96.0	55	90.0	114	93.0
50-59	129	273.3	58	121.0	187	196.6
60-69	235	547.7	174	349.3	409	441.2
70-79	255	923.9	232	637.3	487	760.9
80-89	120	1,212.1	137	815.4	257	962.5
90 and over	18	1,500.0	36	1,090.9	54	1,200.0
Age not stated	2	0.0	2	0.0	4	0.0
TOTAL	**861**	**160.9**	**761**	**138.4**	**1,622**	**149.5**

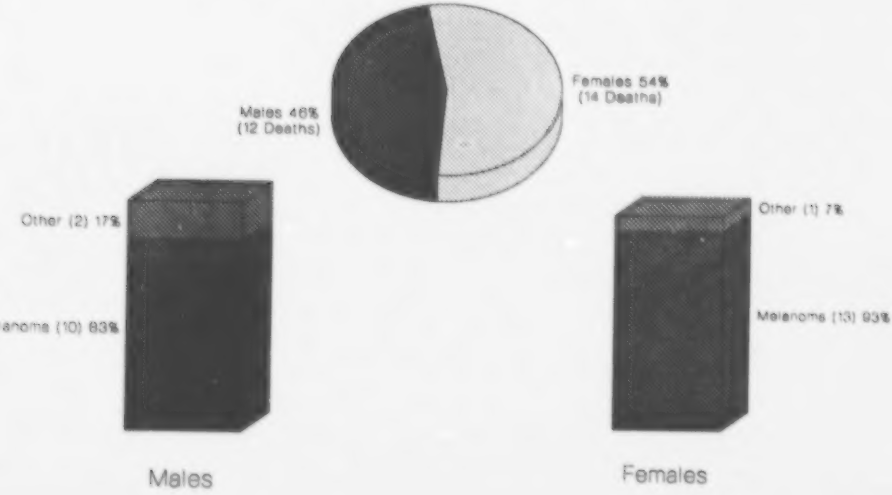
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*1*	*0.3*	*1*	*0.4*	*2*	*0.3*
30-39	*0*	*0.0*	*1*	*1.1*	*1*	*0.5*
40-49	*2*	*3.2*	*2*	*3.2*	*4*	*3.2*
50-59	*0*	*0.0*	*3*	*6.2*	*3*	*3.1*
60-69	*1*	*2.3*	*4*	*8.0*	*5*	*5.3*
70-79	*6*	*21.7*	*2*	*5.4*	*8*	*12.5*
80-89	*2*	*20.2*	*0*	*0.0*	*2*	*7.4*
90 and over	*0*	*0.0*	*1*	*30.3*	*1*	*22.2*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***12***	***2.2***	***14***	***2.5***	***26***	***2.3***

Skin 1988

Incidence



Mortality



Skin (Cont.)

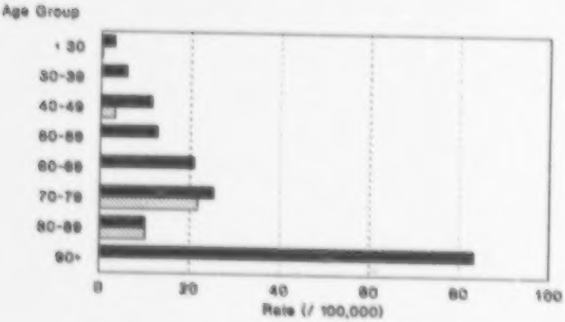
TABLE IXa **MELANOMA 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	8	3.0	4	1.6	12	2.3
30-39	5	5.8	8	9.3	13	7.6
40-49	7	11.4	7	11.4	14	11.4
50-59	6	12.7	5	10.4	11	11.5
60-69	9	20.9	10	20.0	19	20.4
70-79	7	25.3	7	19.2	14	21.8
80-89	1	10.1	6	35.7	7	26.2
90 and over	1	83.3	0	0.0	1	22.2
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**44**	**8.2**	**47**	**8.5**	**91**	**8.3**

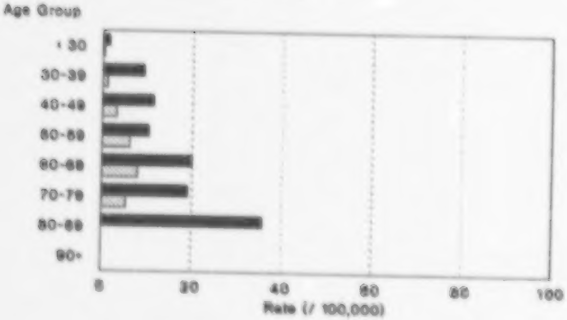
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*1*	*0.3*	*1*	*0.4*	*2*	*0.3*
30-39	*0*	*0.0*	*1*	*1.1*	*1*	*0.5*
40-49	*2*	*3.2*	*2*	*3.2*	*4*	*3.2*
50-59	*0*	*0.0*	*3*	*6.2*	*3*	*3.1*
60-69	*0*	*0.0*	*4*	*8.0*	*4*	*4.3*
70-79	*6*	*21.7*	*2*	*5.4*	*8*	*12.5*
80-89	*1*	*10.1*	*0*	*0.0*	*1*	*3.7*
90 and over	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***10***	***1.8***	***13***	***2.3***	***23***	***2.1***

INCIDENCE & MORTALITY 1988
Melanoma

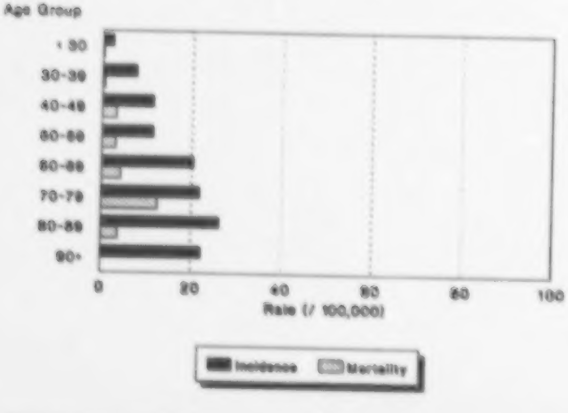
Males



Females



Total Population



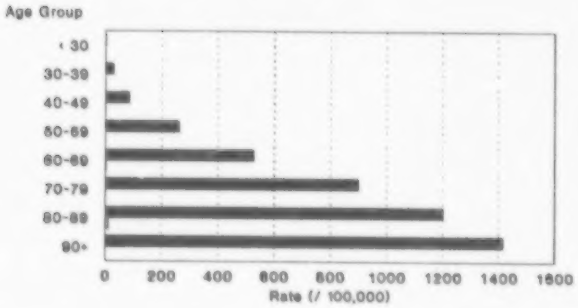
Skin (Cont.)

TABLE IXb **OTHER MALIGNANT NEOPLASMS 1988**

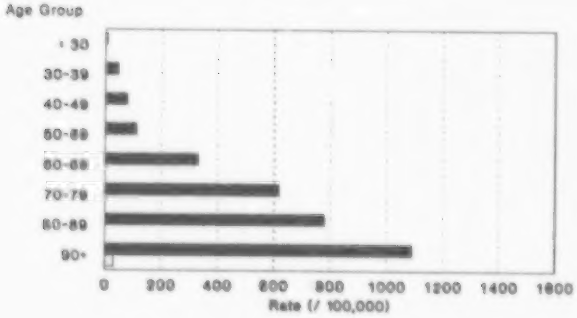
INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	6	2.3	17	6.8	23	4.5
30-39	24	28.0	38	44.4	62	36.2
40-49	52	84.6	48	78.5	100	81.6
50-59	123	260.5	53	110.6	176	185.0
60-69	226	526.8	164	329.3	390	420.7
70-79	248	898.5	225	618.1	473	739.0
80-89	119	1,202.0	131	779.7	250	936.3
90 and over	17	1,416.6	36	1,090.9	53	1,177.7
Age not stated	2	0.0	2	0.0	4	0.0
TOTAL	**817**	**152.7**	**714**	**129.8**	**1,531**	**141.0**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
50-59	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
60-69	*1*	*2.3*	*0*	*0.0*	*1*	*1.0*
70-79	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
80-89	*1*	*10.1*	*0*	*0.0*	*1*	*3.7*
90 and over	*0*	*0.0*	*1*	*30.3*	*1*	*22.2*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***2***	***0.3***	***1***	***0.1***	***3***	***0.2***

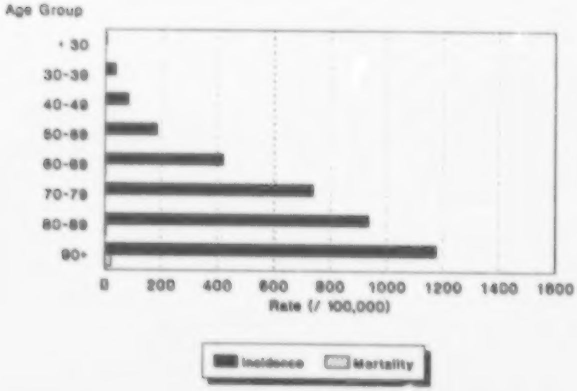
INCIDENCE & MORTALITY 1988
Other Malignant Neoplasms
Skin
Males



Females



Total Population



INCIDENCE & MORTALITY 1988

Brain & Nervous System

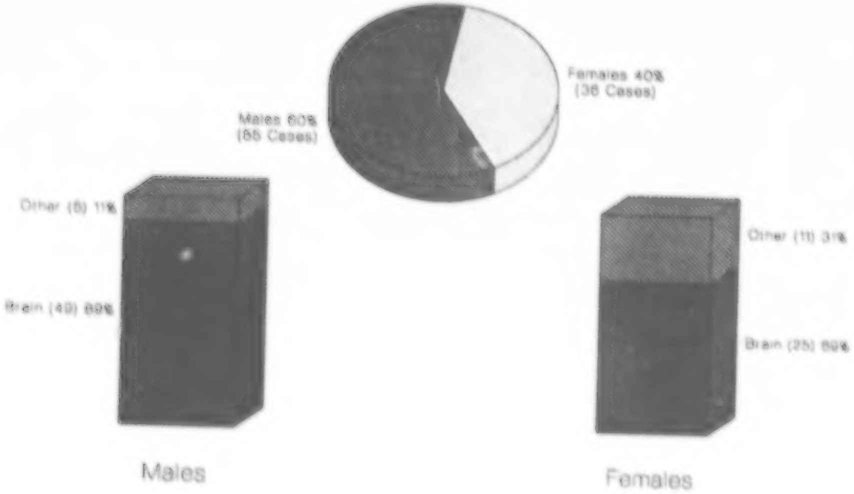
TABLE X **BRAIN and NERVOUS SYSTEM 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	8	3.0	4	1.6	12	2.3
30-39	6	7.0	4	4.6	10	5.8
40-49	7	11.4	2	3.2	9	7.3
50-59	6	12.7	6	12.5	12	12.6
60-69	17	39.6	8	16.0	25	26.9
70-79	9	32.6	9	24.7	18	28.1
80-89	2	20.2	3	17.8	5	18.7
90 and over	0	0.0	0	0.0	0	0.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**55**	**10.2**	**36**	**6.5**	**91**	**8.3**

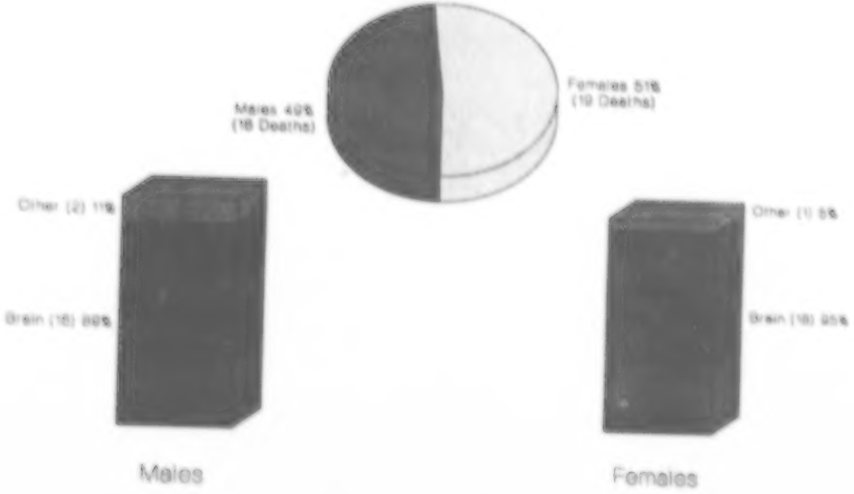
MORTALITY	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	4	1.5	0	0.0	4	0.7
30-39	3	3.5	1	1.1	4	2.3
40-49	0	0.0	2	3.2	2	1.6
50-59	4	8.4	5	10.4	9	9.4
60-69	4	9.3	4	8.0	8	8.6
70-79	2	7.2	6	16.4	8	12.5
80-89	0	0.0	1	5.9	1	3.7
90 and over	1	83.3	0	0.0	1	22.2
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**18**	**3.3**	**19**	**3.4**	**37**	**3.4**

Brain & Nervous System 1988

Incidence



Mortality



Brain and Nervous System (Cont.)

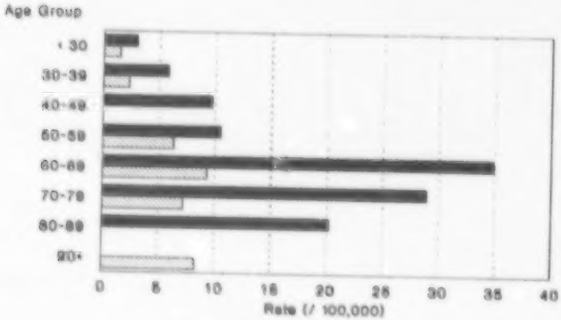
TABLE Xa **BRAIN 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	8	3.0	3	1.2	11	2.1
30-39	5	5.8	2	2.3	7	4.0
40-49	6	9.7	1	1.6	7	5.7
50-59	5	10.5	5	10.4	10	10.5
60-69	15	34.9	5	10.0	20	21.5
70-79	8	28.9	7	19.2	15	23.4
80-89	2	20.2	2	11.9	4	14.9
90 and over	0	0.0	0	0.0	0	0.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**49**	**9.1**	**25**	**4.5**	**74**	**6.8**

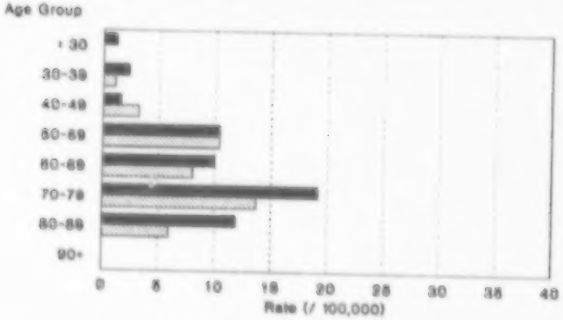
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*4*	*1.5*	*0*	*0.0*	*4*	*0.7*
30-39	*2*	*2.3*	*1*	*1.1*	*3*	*1.7*
40-49	*0*	*0.0*	*2*	*3.2*	*2*	*1.6*
50-59	*3*	*6.3*	*5*	*10.4*	*8*	*8.4*
60-69	*4*	*9.3*	*4*	*8.0*	*8*	*8.6*
70-79	*2*	*7.2*	*5*	*13.7*	*7*	*10.9*
80-89	*0*	*0.0*	*1*	*5.9*	*1*	*3.7*
90 and over	*1*	*83.3*	*0*	*0.0*	*1*	*22.2*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***16***	***2.9***	***18***	***3.2***	***34***	***3.1***

INCIDENCE & MORTALITY 1988
Brain

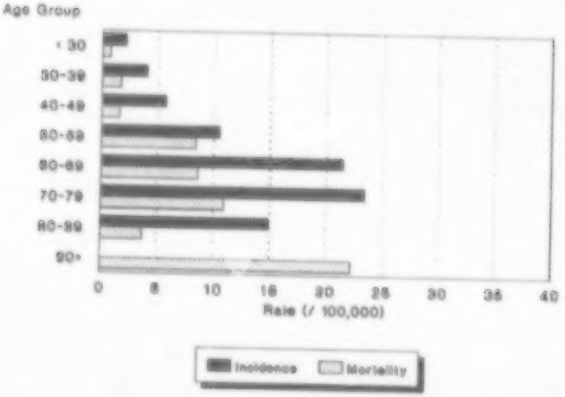
Males



Females



Total Population



Thyroid & Endocrine Glands 1988

TABLE XI **THYROID AND ENDOCRINE GLANDS 1988**

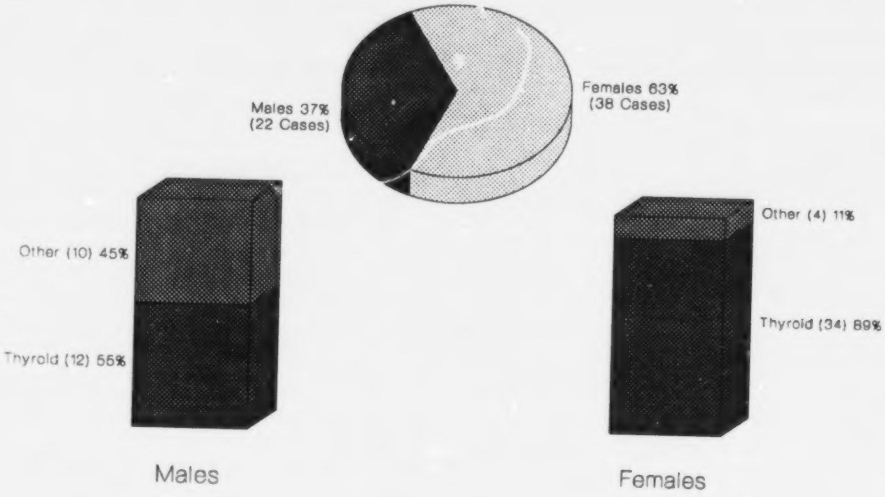
INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	2	0.7	5	2.0	7	1.3
30-39	4	4.6	6	7.0	10	5.8
40-49	2	3.2	7	11.4	9	7.3
50-59	5	10.5	7	14.6	12	12.6
60-69	7	16.3	4	8.0	11	11.8
70-79	1	3.6	8	21.9	9	14.0
80-89	1	10.1	1	5.9	2	7.4
90 and over	0	0.0	0	0.0	0	0.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**22**	**4.1**	**38**	**6.9**	**60**	**5.5**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*1*	*0.3*	*1*	*0.4*	*2*	*0.3*
30-39	*0*	*0.0*	*3*	*3.5*	*3*	*1.7*
40-49	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
50-59	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
60-69	*3*	*6.9*	*1*	*2.0*	*4*	*4.3*
70-79	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
80-89	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
90 and over	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***4***	***0.7***	***5***	***0.9***	***9***	***0.8***

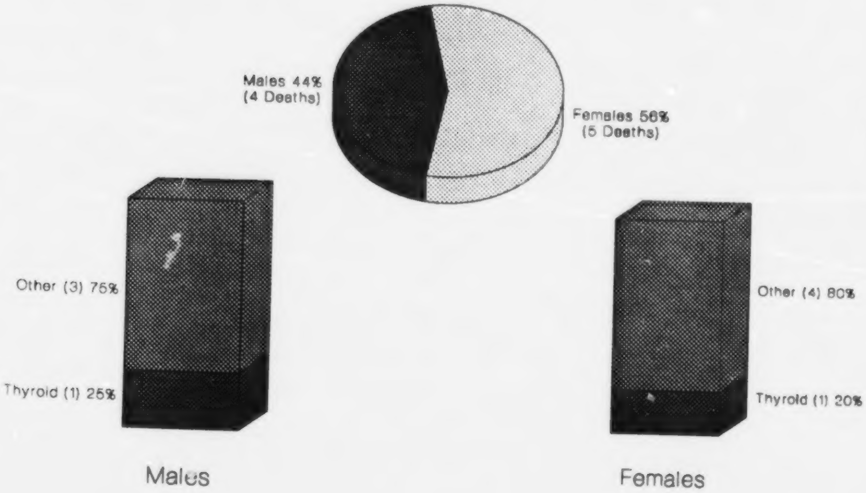
INCIDENCE & MORTALITY 1988

Thyroid & Endocrine Glands

Incidence



Mortality



Thyroid and Endocrine Glands (Cont.

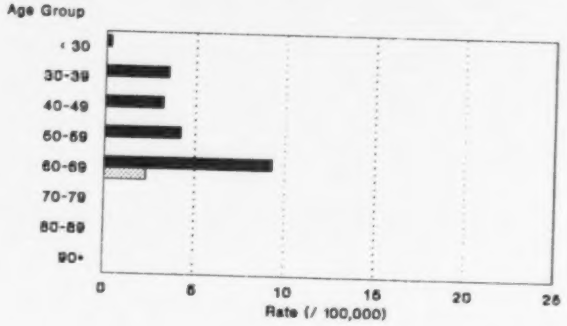
TABLE XIa **THYROID 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	1	0.3	4	1.6	5	0.9
30-39	3	3.5	4	4.6	7	4.0
40-49	2	3.2	7	11.4	9	7.3
50-59	2	4.2	7	14.6	9	9.4
60-69	4	9.3	4	8.0	8	8.6
70-79	0	0.0	7	19.2	7	10.9
80-89	0	0.0	1	5.9	1	3.7
90 and over	0	0.0	0	0.0	0	0.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**12**	**2.2**	**34**	**6.1**	**46**	**4.2**

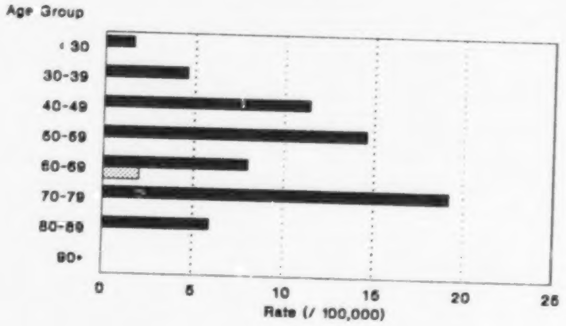
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
50-59	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
60-69	*1*	*2.3*	*1*	*2.0*	*2*	*2.1*
70-79	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
80-89	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
90 and over	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***1***	***0.1***	***1***	***0.1***	***2***	***0.1***

INCIDENCE & MORTALITY 1988
Thyroid

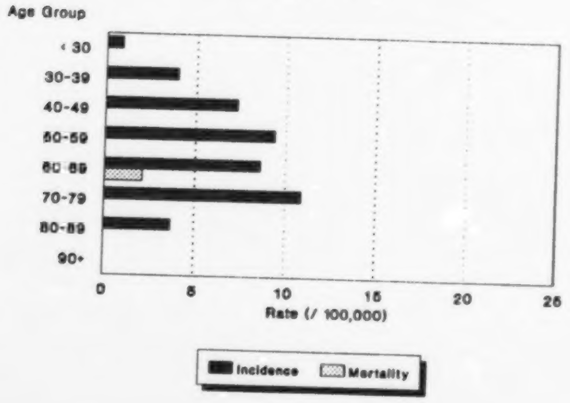
Males



Females



Total Population



INCIDENCE & MORTALITY 1988

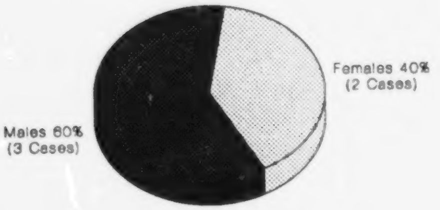
Bone

TABLE XII **BONE 1988**

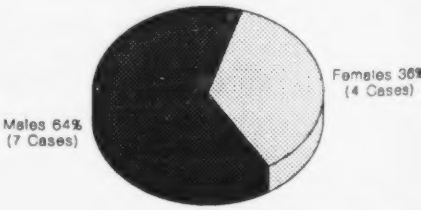
INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	0	0.0	1	0.4	1	0.1
30-39	0	0.0	0	0.0	0	0.0
40-49	1	1.6	0	0.0	1	0.8
50-59	1	2.1	0	0.0	1	1.0
60-69	0	0.0	1	2.0	1	1.0
70-79	0	0.0	0	0.0	0	0.0
80-89	1	10.1	0	0.0	1	3.7
90 and over	0	0.0	0	0.0	0	0.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**3**	**0.5**	**2**	**0.3**	**5**	**0.4**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
40-49	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
50-59	*2*	*4.2*	*0*	*0.0*	*2*	*2.1*
60-69	*2*	*4.6*	*1*	*2.0*	*3*	*3.2*
70-79	*2*	*7.2*	*2*	*5.4*	*4*	*6.2*
80-89	*1*	*10.1*	*1*	*5.9*	*2*	*7.4*
90 and over	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***7***	***1.3***	***4***	***0.7***	***11***	***1.0***

Incidence



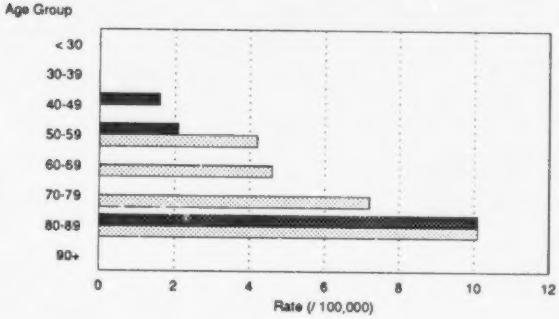
Mortality



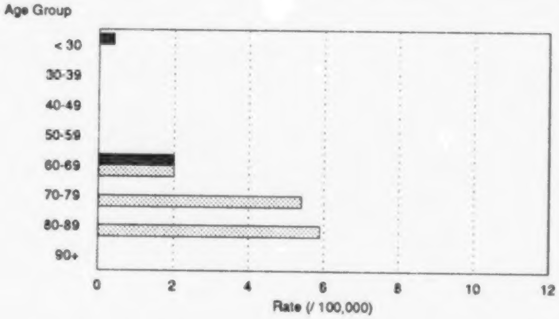
INCIDENCE & MORTALITY 1988

Bone

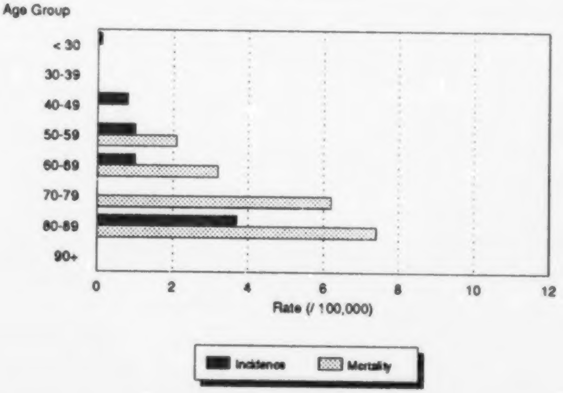
Males



Females



Total Population



INCIDENCE & MORTALITY 1988

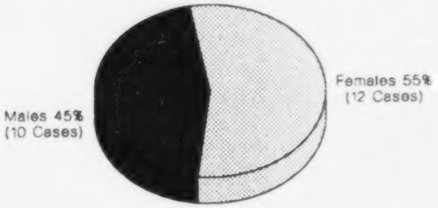
Connective Tissue

TABLE XIII **CONNECTIVE TISSUE 1988**

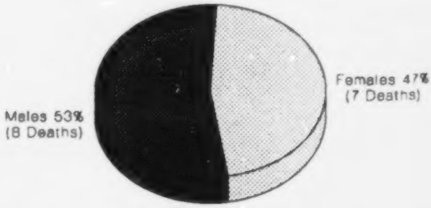
INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	4	1.5	3	1.2	7	1.3
30-39	1	1.1	1	1.1	2	1.1
40-49	1	1.6	1	1.6	2	1.6
50-59	0	0.0	1	2.0	1	1.0
60-69	1	2.3	1	2.0	2	2.1
70-79	3	10.8	2	5.4	5	7.8
80-89	0	0.0	2	11.9	2	7.4
90 and over	0	0.0	1	30.3	1	22.2
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**10**	**1.8**	**12**	**2.1**	**22**	**2.0**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*1*	*0.3*	*0*	*0.0*	*1*	*0.1*
30-39	*0*	*0.0*	*2*	*2.3*	*2*	*1.1*
40-49	*1*	*1.6*	*0*	*0.0*	*1*	*0.8*
50-59	*2*	*4.2*	*1*	*2.0*	*3*	*3.1*
60-69	*1*	*2.3*	*1*	*2.0*	*2*	*2.1*
70-79	*2*	*7.2*	*2*	*5.4*	*4*	*6.2*
80-89	*1*	*10.1*	*1*	*5.9*	*2*	*7.4*
90 and over	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***8***	***1.4***	***7***	***1.2***	***15***	***1.3***

Incidence

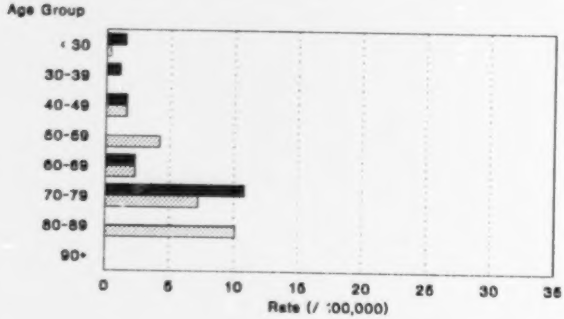


Mortality

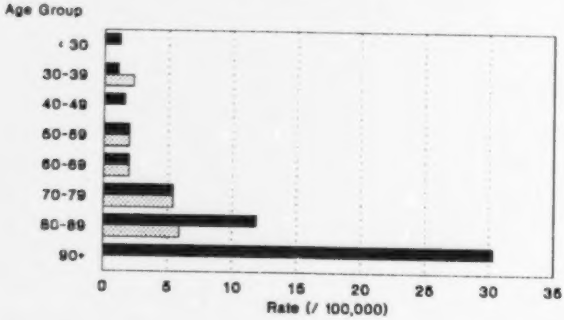


INCIDENCE & MORTALITY 1988
Connective Tissue

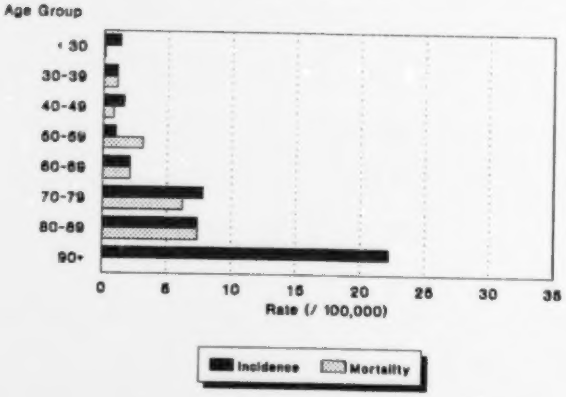
Males



Females



Total Population



INCIDENCE & MORTALITY 1988

Lymphatic & Haematopoietic Systems

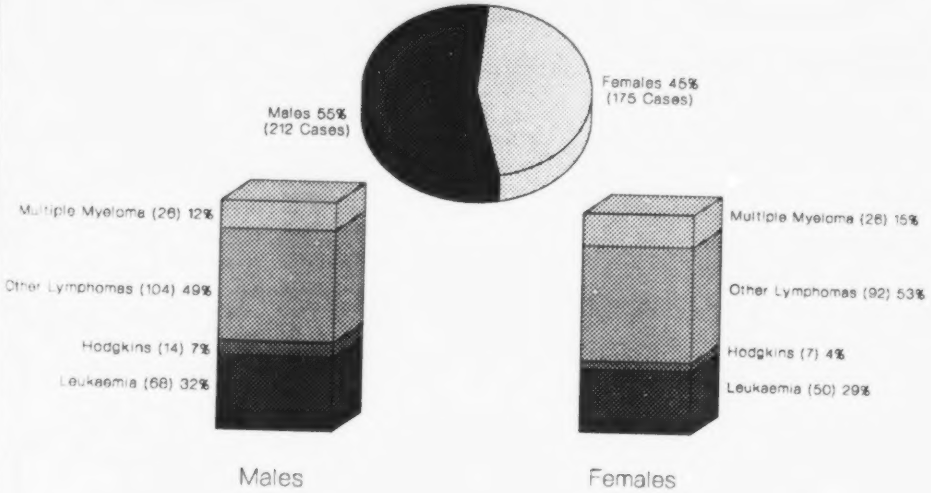
TABLE XIV **LYMPHATIC & HAEMATOPOIETIC SYSTEMS 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	23	8.8	14	5.6	37	7.2
30-39	17	19.8	14	16.3	31	18.1
40-49	21	34.2	12	19.6	33	26.9
50-59	26	55.0	15	31.3	41	43.1
60-69	46	107.2	39	78.3	85	91.6
70-79	60	217.3	48	131.8	108	168.7
80-89	17	171.7	29	172.6	46	172.2
90 and over	2	166.6	4	121.2	6	133.3
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**212**	**39.6**	**175**	**31.8**	**387**	**35.6**

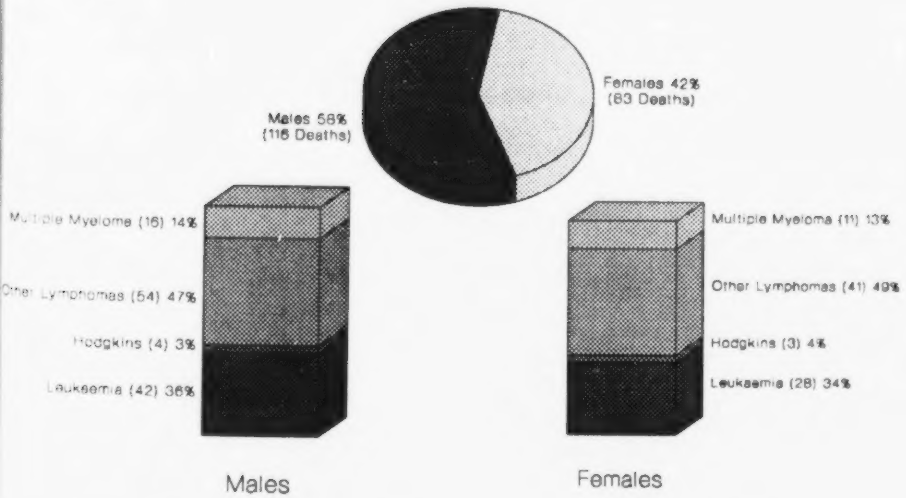
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*6*	*2.3*	*3*	*1.2*	*9*	*1.7*
30-39	*6*	*7.0*	*0*	*0.0*	*6*	*3.5*
40-49	*10*	*16.2*	*2*	*3.2*	*12*	*9.7*
50-59	*5*	*10.5*	*7*	*14.6*	*12*	*12.6*
60-69	*20*	*46.6*	*16*	*32.1*	*36*	*38.8*
70-79	*42*	*152.1*	*26*	*71.4*	*68*	*106.2*
80-89	*21*	*212.1*	*27*	*160.7*	*48*	*179.7*
90 and over	*6*	*500.0*	*2*	*60.6*	*8*	*177.7*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***116***	***21.6***	***83***	***15.0***	***199***	***18.3***

Lymphatic & Haematopoietic 1988

Incidence



Mortality



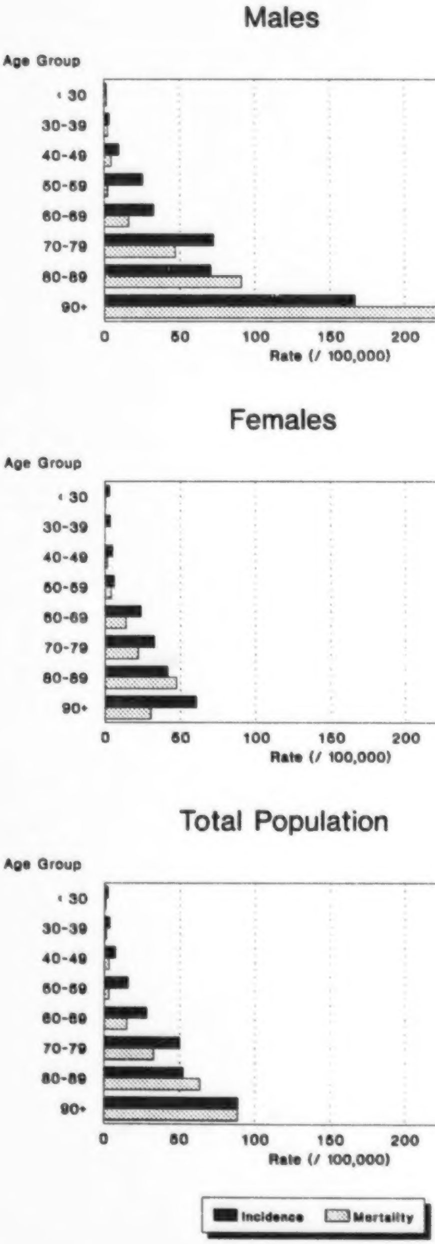
Lymphatic & Haematopoietic Systems

TABLE XIVa **LEUKAEMIA 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	4	1.5	8	3.2	12	2.3
30-39	3	3.5	3	3.5	6	3.5
40-49	6	9.7	3	4.9	9	7.3
50-59	12	25.4	3	6.2	15	15.7
60-69	14	32.6	12	24.0	26	28.0
70-79	20	72.4	12	32.9	32	50.0
80-89	7	70.7	7	41.6	14	52.4
90 and over	2	166.6	2	60.6	4	88.8
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**68**	**12.7**	**50**	**9.0**	**118**	**10.8**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*4*	*1.5*	*1*	*0.4*	*5*	*0.9*
30-39	*2*	*2.3*	*0*	*0.0*	*2*	*1.1*
40-49	*3*	*4.8*	*1*	*1.6*	*4*	*3.2*
50-59	*1*	*2.1*	*2*	*4.1*	*3*	*3.1*
60-69	*7*	*16.3*	*7*	*14.0*	*14*	*15.1*
70-79	*13*	*47.1*	*8*	*21.9*	*21*	*32.8*
80-89	*9*	*90.9*	*8*	*47.6*	*17*	*63.6*
90 and over	*3*	*250.0*	*1*	*30.3*	*4*	*88.8*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***42***	***7.8***	***28***	***5.0***	***70***	***6.4***

INCIDENCE & MORTALITY 1988
Leukaemia


Males

Females

Total Population

Lymphatic & Haematopoietic Systems

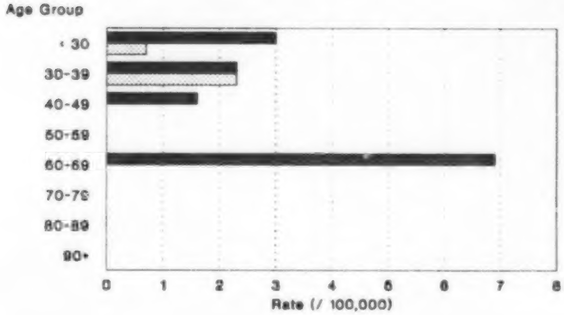
TABLE XIVb **HODGKINS DISEASE 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	8	3.0	3	1.2	11	2.1
30-39	2	2.3	2	2.3	4	2.3
40-49	1	1.6	1	1.6	2	1.6
50-59	0	0.0	1	2.0	1	1.0
60-69	3	6.9	0	0.0	3	3.2
70-79	0	0.0	0	0.0	0	0.0
80-89	0	0.0	0	0.0	0	0.0
90 and over	0	0.0	0	0.0	0	0.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**14**	**2.6**	**7**	**1.2**	**21**	**1.9**

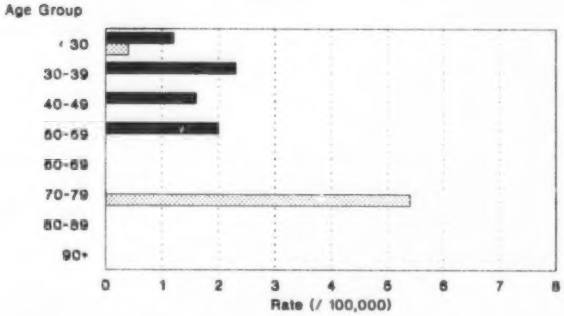
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*2*	*0.7*	*1*	*0.4*	*3*	*0.5*
30-39	*2*	*2.3*	*0*	*0.0*	*2*	*1.1*
40-49	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
50-59	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
60-69	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
70-79	*0*	*0.0*	*2*	*5.4*	*2*	*3.1*
80-89	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
90 and over	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***4***	***0.7***	***3***	***0.5***	***7***	***0.6***

INCIDENCE & MORTALITY 1988
Hodgkins Disease

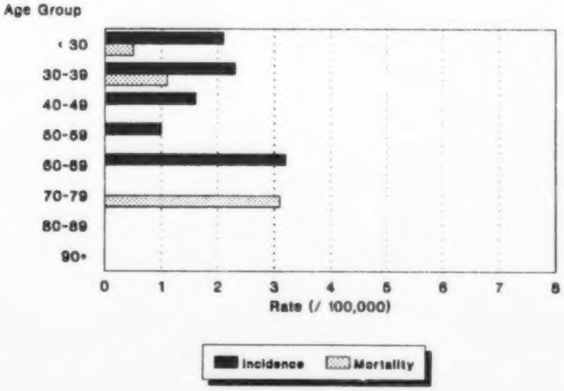
Males



Females



Total Population



Lymphatic & Haematopoietic Systems

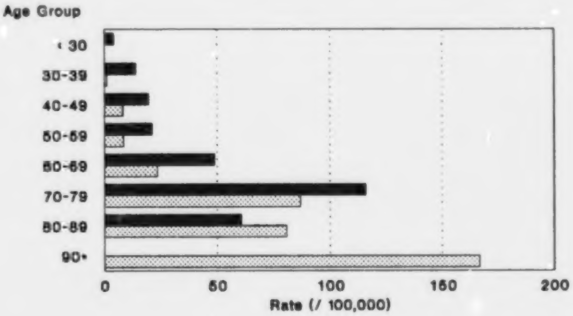
TABLE XIVc **LYMPHOMAS 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	11	4.2	3	1.2	14	2.7
30-39	12	14.0	7	8.1	19	11.1
40-49	12	19.5	6	9.8	18	14.6
50-59	10	21.1	9	18.7	19	19.9
60-69	21	48.9	21	42.1	42	45.3
70-79	32	115.9	27	74.1	59	92.1
80-89	6	60.6	17	101.1	23	86.1
90 and over	0	0.0	2	60.6	2	44.4
Age not stated	0	0.0	0	0.0	0	0.0
Total	104	19.4	92	16.7	196	18.0

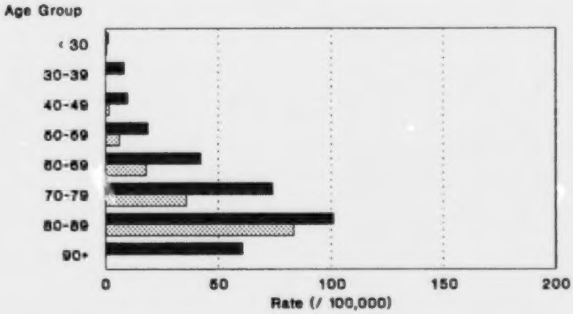
MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*1*	*0.4*	*1*	*0.1*
30-39	*1*	*1.1*	*0*	*0.0*	*1*	*0.5*
40-49	*5*	*8.1*	*1*	*1.6*	*6*	*4.8*
50-59	*4*	*8.4*	*3*	*6.2*	*7*	*7.3*
60-69	*10*	*23.3*	*9*	*18.0*	*19*	*20.4*
70-79	*24*	*86.9*	*13*	*35.7*	*37*	*57.8*
80-89	*8*	*80.8*	*14*	*83.3*	*22*	*82.3*
90 and over	*2*	*166.6*	*0*	*0.0*	*2*	*44.4*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
Total	*54*	*10.0*	*41*	*7.4*	*95*	*8.7*

INCIDENCE & MORTALITY 1988
Lymphomas

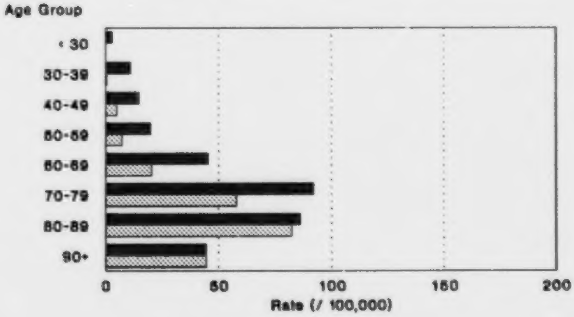
Males



Females



Total Population



▇ Incidence ▨ Mortality

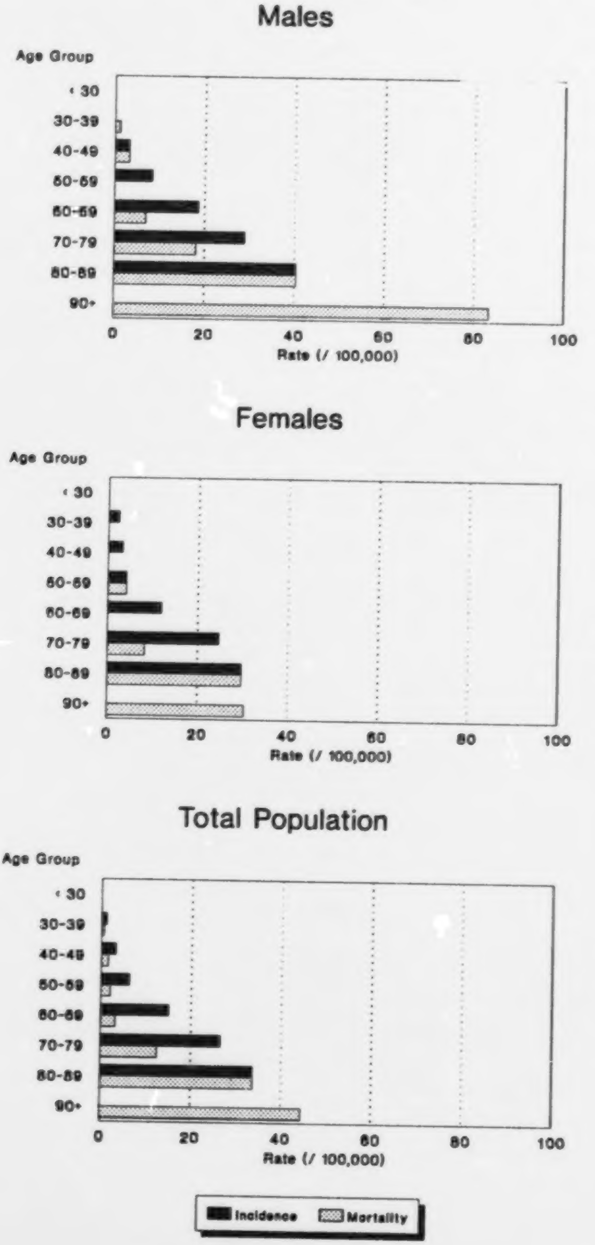
Lymphatic & Haematopoietic Systems

TABLE XIVd **MULTIPLE MYELOMA 1988**

INCIDENCE	**Male**	**Rate**	**Female**	**Rate**	**TOTAL**	**RATE**
Under 30	0	0.0	0	0.0	0	0.0
30-39	0	0.0	2	2.3	2	1.1
40-49	2	3.2	2	3.2	4	3.2
50-59	4	8.4	2	4.1	6	6.3
60-69	8	18.6	6	12.0	14	15.1
70-79	8	28.9	9	24.7	17	26.5
80-89	4	40.4	5	29.7	9	33.7
90 and over	0	0.0	0	0.0	0	0.0
Age not stated	0	0.0	0	0.0	0	0.0
TOTAL	**26**	**4.8**	**26**	**4.7**	**52**	**4.7**

MORTALITY	***Male***	***Rate***	***Female***	***Rate***	***TOTAL***	***RATE***
Under 30	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
30-39	*1*	*1.1*	*0*	*0.0*	*1*	*0.5*
40-49	*2*	*3.2*	*0*	*0.0*	*2*	*1.6*
50-59	*0*	*0.0*	*2*	*4.1*	*2*	*2.1*
60-69	*3*	*6.9*	*0*	*0.0*	*3*	*3.2*
70-79	*5*	*18.1*	*3*	*8.2*	*8*	*12.5*
80-89	*4*	*40.4*	*5*	*29.7*	*9*	*33.7*
90 and over	*1*	*83.3*	*1*	*30.3*	*2*	*44.4*
Age not stated	*0*	*0.0*	*0*	*0.0*	*0*	*0.0*
TOTAL	***16***	***2.9***	***11***	***2.0***	***27***	***2.4***

INCIDENCE & MORTALITY 1988
Multiple Myeloma



INCIDENCE & MORTALITY 1988

Female Genital Organs

TABLE XVa **FEMALE GENITAL ORGANS 1988**

INCIDENCE

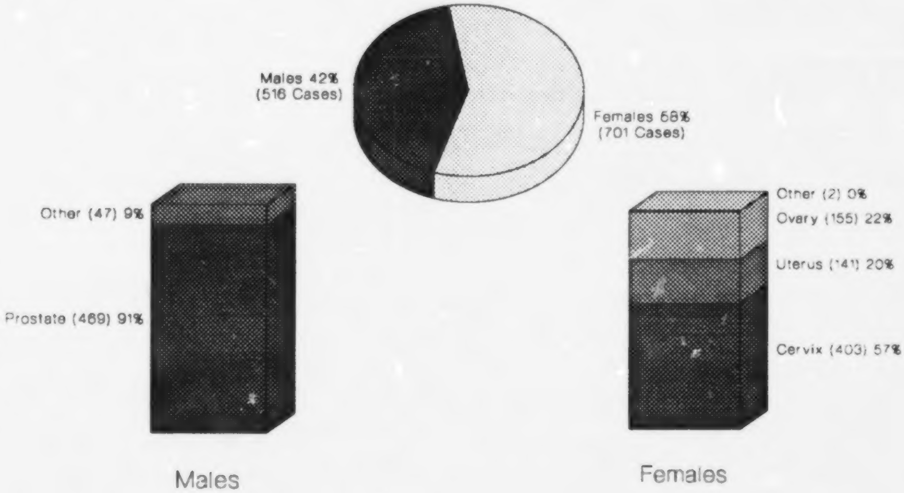
All Organs	N	Rate	Cervix Uteri	N	Rate
Under 30	171	68.6	Under 30	162	65.0
30-39	178	208.1	30-39	150	175.4
40-49	56	94.9	40-49	38	62.1
50-59	71	148.2	50-59	18	37.5
60-69	117	234.9	60-69	18	36.1
70-79	68	186.8	70-79	8	21.9
80-89	33	196.4	80-89	6	35.7
90 and over	7	212.1	90 and over	3	90.9
Age not stated	0	0.0	Age not stated	0	0.0
TOTAL	**701**	**127.5**	**TOTAL**	**403**	**73.2**

MORTALITY

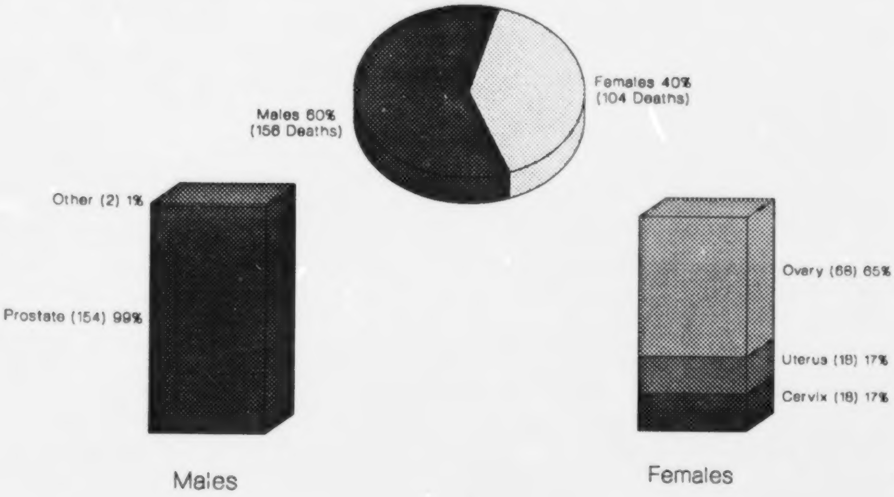
All Organs	*N*	*Rate*	*Cervix Uteri*	*N*	*Rate*
Under 30	*0*	*0.0*	*Under 30*	*0*	*0.0*
30-39	*3*	*3.5*	*30-39*	*3*	*3.5*
40-49	*5*	*8.1*	*40-49*	*4*	*6.5*
50-59	*13*	*27.1*	*50-59*	*3*	*6.2*
60-69	*28*	*56.2*	*60-69*	*5*	*10.0*
70-79	*37*	*101.6*	*70-79*	*2*	*5.4*
80-89	*13*	*77.3*	*80-89*	*0*	*0.0*
90 and over	*5*	*151.5*	*90 and over*	*1*	*30.3*
Age not stated	*0*	*0.0*	*Age not stated*	*0*	*0.0*
TOTAL	***104***	***18.9***	***TOTAL***	***18***	***3.2***

Genital Organs 1988

Incidence



Mortality



Female Genital Organs (Cont.)

TABLE XVb **FEMALE GENITAL ORGANS 1988**

INCIDENCE

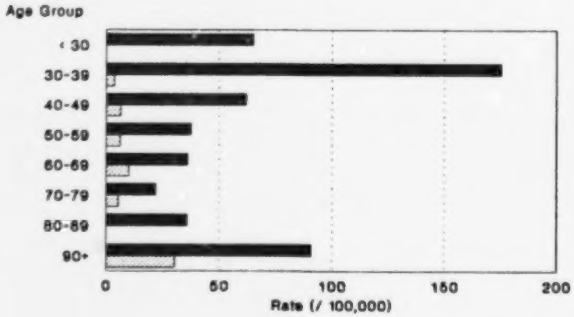
Uterus- Corpus Etc. (Except Cervix)			Ovaries,Fallopian- Tubes,Broad Ligaments & Other Genital Organs		
Under 30	2	0.8	Under 30	5	2.0
30-39	6	7.1	30-39	22	25.7
40-49	7	11.4	40-49	11	18.0
50-59	21	43.8	50-59	32	66.8
60-69	58	116.4	60-69	41	82.3
70-79	34	93.4	70-79	25	66.8
80-89	11	65.4	80-89	16	95.2
90 and over	2	60.6	90 and over	3	90.9
Age not stated	0	0.0	Age not stated	0	0.0
TOTAL	**141**	**25.6**	**TOTAL**	**155**	**28.1**

MORTALITY

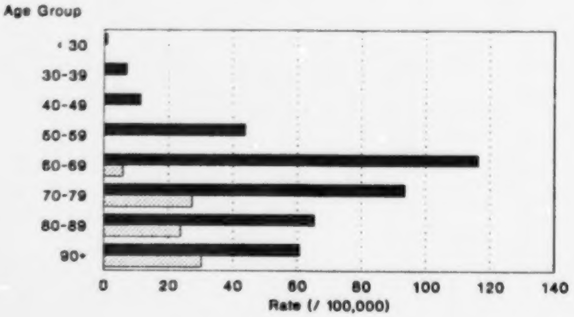
Uterus- Corpus Etc. (Except Cervix)			*Ovaries,Fallopian- Tubes,Broad Ligaments & Other Genital Organ*		
Under 30	*0*	*0.0*	*Under 30*	*0*	*0.0*
30-39	*0*	*0.0*	*30-39*	*0*	*0.0*
40-49	*0*	*0.0*	*40-49*	*1*	*1.6*
50-59	*0*	*0.0*	*50-59*	*10*	*20.8*
60-69	*3*	*6.0*	*60-69*	*20*	*40.1*
70-79	*10*	*27.4*	*70-79*	*25*	*68.6*
80-89	*4*	*23.8*	*80-89*	*9*	*53.5*
90 and over	*1*	*30.3*	*90 and over*	*3*	*90.9*
Age not stated	*0*	*0.0*	*Age not stated*	*0*	*0.0*
TOTAL	***18***	***3.2***	***TOTAL***	***68***	***12.3***

INCIDENCE & MORTALITY 1988
Female Genital Organs

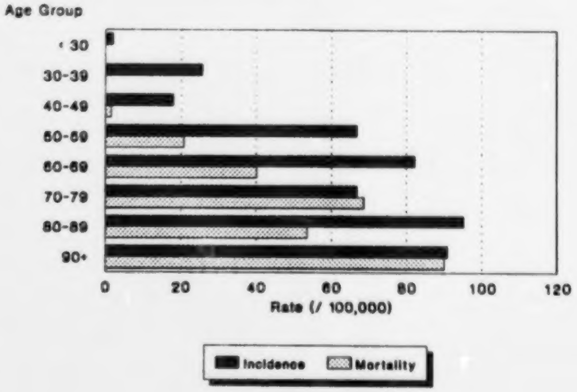
Cervix



Uterus



Ovary



INCIDENCE & MORTALITY 1988
Male Genital Organs

TABLE XVIa **MALE GENITAL ORGANS 1988**

INCIDENCE

All Organs	N	Rate	Prostate	N	Rate
Under 30	14	5.4	Under 30	0	0.0
30-39	13	15.2	30-39	0	0.0
40-49	14	22.8	40-49	5	8.1
50-59	26	55.0	50-59	21	44.4
60-69	110	256.4	60-69	108	251.7
70-79	225	815.2	70-79	223	807.9
80-89	97	979.7	80-89	96	969.6
90 and over	17	1,416.6	90 and over	16	1,333.3
Age not stated	0	0.0	Age not stated	0	0.0
TOTAL	**516**	**96.4**	**TOTAL**	**469**	**87.6**

MORTALITY

All Organs	*N*	*Rate*	*Prostate*	*N*	*Rate*
Under 30	*0*	*0.0*	*Under 30*	*0*	*0.0*
30-39	*0*	*0.0*	*30-39*	*0*	*0.0*
40-49	*1*	*1.6*	*40-49*	*0*	*0.0*
50-59	*6*	*12.7*	*50-59*	*6*	*12.7*
60-69	*26*	*60.6*	*60-69*	*26*	*60.6*
70-79	*58*	*210.1*	*70-79*	*58*	*210.1*
80-89	*50*	*505.0*	*80-89*	*49*	*494.9*
90 and over	*15*	*1,250.0*	*90 and over*	*15*	*1,250.0*
Age not stated	*0*	*0.0*	*Age not stated*	*0*	*0.0*
TOTAL	***156***	***29.1***	***TOTAL***	***154***	***28.7***

TABLE XVIb **MALE GENITAL ORGANS 1988**

INCIDENCE			*MORTALITY*		
Other Genital Organs	**N**	**Rate**	***Other Genital Organs***	***N***	***Rate***
Under 30	14	5.4	*Under 30*	*0*	*0.0*
30-39	13	15.2	*30-39*	*0*	*0.0*
40-49	9	14.6	*40-49*	*1*	*1.6*
50-59	5	10.5	*50-59*	*0*	*0.0*
60-69	2	4.6	*60-69*	*0*	*0.0*
70-79	2	7.2	*70-79*	*0*	*0.0*
80-89	1	10.1	*80-89*	*1*	*10.1*
90 and over	1	83.3	*90 and over*	*0*	*0.0*
Age not stated	0	0.0	*Age not stated*	*0*	*0.0*
TOTAL	**47**	**8.7**	***TOTAL***	***2***	***0.3***

INCIDENCE & MORTALITY 1988

Prostate

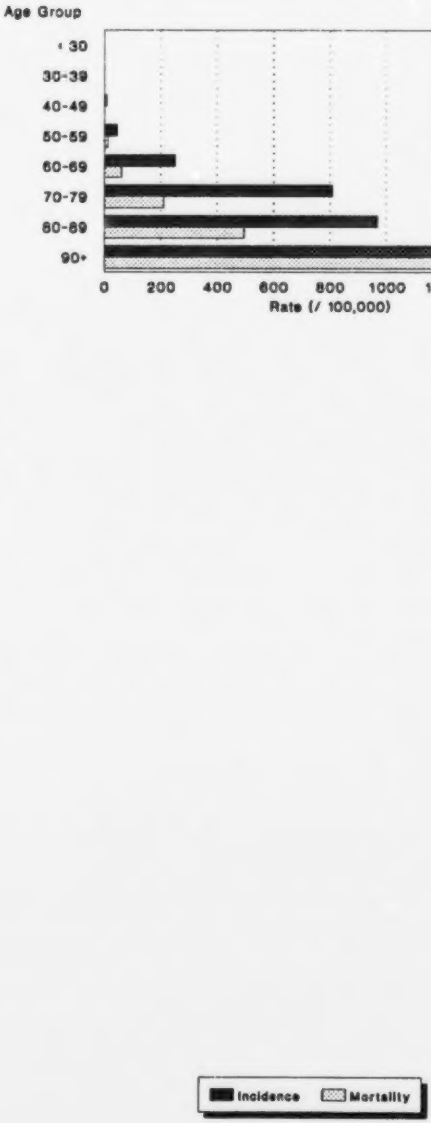


TABLE XVIIa **CANCER INCIDENCE - BY SITE**

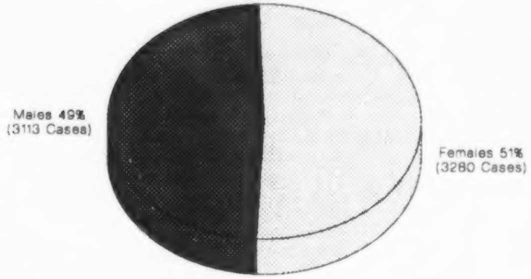
ICDA 9th Rev.	Site	Male	Female	Total
140	Lip	55	10	65
141	Tongue	13	10	23
142	Salivary Glands	5	0	5
143	Gums	1	2	3
144	Floor of the Mouth	7	8	15
145	Other Parts of Mouth	5	1	6
146	Oropharynx	18	5	23
147	Nasopharynx	4	5	9
148	Hypopharynx	6	2	8
149	Pharynx Unspecified	4	1	5
150	Oesophagus	34	14	48
151	Stomach	105	54	159
152	Small Intestines	4	7	11
153	Large Intestines	231	263	494
154	Rectum and Rectosigmoid Junction	110	113	223
155	Liver and Intrahepatic Ducts	10	7	17
156	Gall Bladder and Extrahepatic Ducts	17	20	37
157	Pancreas	61	53	114
158	Peritoneum and Retroperitoneal Tissue	4	10	14
159	Digestive - N.O.S.	1	0	1
160	Nose,Nasal Cavities, Ear and Accessory	6	3	9
161	Larynx	39	7	46
162	Trachea,Bronchus and Lung	469	206	675
163-165	Other and Unspecified Respiratory Organs	11	5	16
170	Bones	3	2	5
171	Connective Tissue	10	12	22

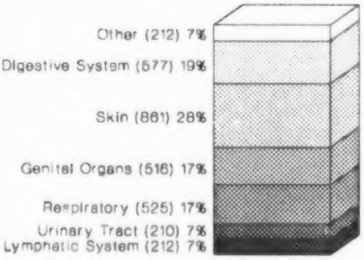
TABLE XVIIb CANCER INCIDENCE - BY SITE

ICDA 9th Rev.	Site	Male	Female	Total
172	Malignant Melanoma of Skin	44	47	91
173	Malignant Neoplasm of Skin	817	714	1,531
174-175	Breast	7	645	652
179-182	Uterus-Corpus Except Cervix	0	141	141
180,233.1	Cervix Uteri	0	403	403
183	Ovary,Fallopian Tubes and Broad Ligaments	0	89	89
184,236.1	Other Female Genital Organs	0	61	61
185	Prostate	469	0	469
186	Testis	27	0	27
187	Other Male Genital Organs	15	0	15
188	Bladder	132	61	193
189	Other and Unspecified Urinary Organs	74	42	116
190	Eye	5	6	11
191	Brain	49	25	74
192	Other Parts of Nervous System	1	5	6
193	Thyroid Gland	12	34	46
194,164.0	Endocrine Gland	10	4	14
195-9	Other and Unspecified Sites	85	67	152
200	Lymphasarcoma and Reticulosarcoma	49	41	90
201	Hodgkins Disease	14	7	21
202	Other Lymphomas (Recticulosis)	55	51	106
203	Multiple Myeloma	26	26	52
204-8	Leukaemia	68	50	118
238.4	Polycythemia Vera	6	6	12
289.0	Myelofibrosis	6	1	7
	Total - All Sites	**3,204**	**3,346**	**6,550**

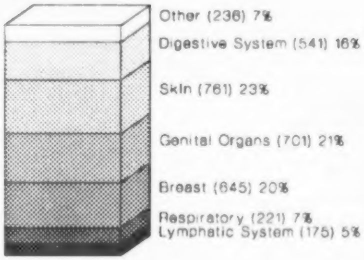
ALL SITES 1988

Incidence





Males



Females

Other (# Cases):

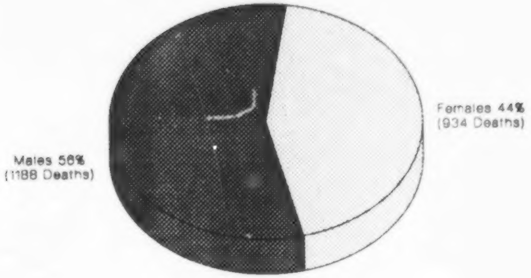
Buccal Cavity ... 115
Thyroid ... 22
Brain ... 55
Connective Tissue ... 10
Bone ... 3
Breast ... 7

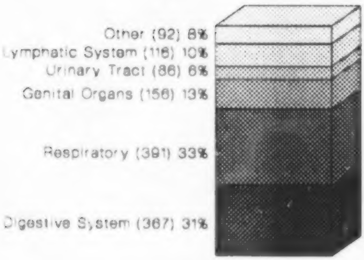
Other (# Cases):

Buccal Cavity ... 44
Thyroid ... 38
Brain ... 36
Connective Tissue ... 12
Bone ... 2
Urinary Tract ... 104

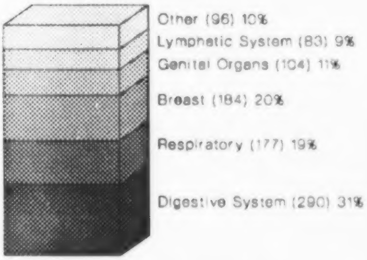
ALL SITES 1988

Mortality





Males



Females

Other (# Cases):
Buccal Cavity ... 40
Breast ... 3
Skin ... 12
Brain ... 18
Thyroid ... 4
Bone ... 7
Connective Tissue ... 8

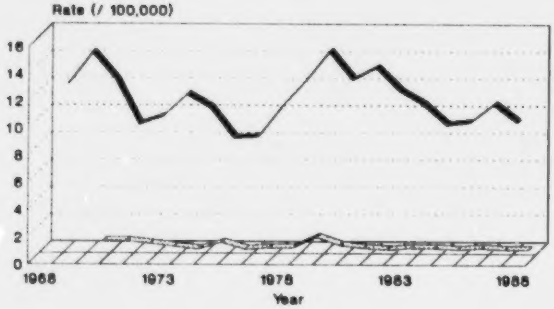
Other (# Cases):
Buccal Cavity ... 7
Urinary Tract ... 40
Skin ... 14
Brain ... 19
Throid ... 5
Bone ... 4
Connective Tissue ... 7

20-YEAR
TRENDS

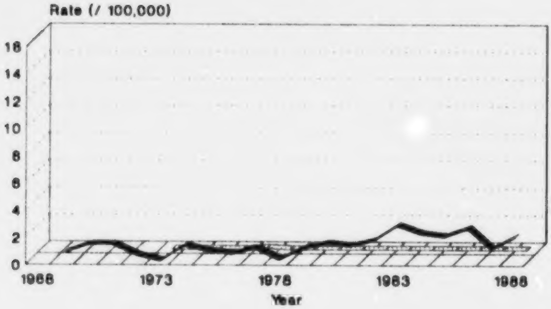
20-YEAR TRENDS

Lip

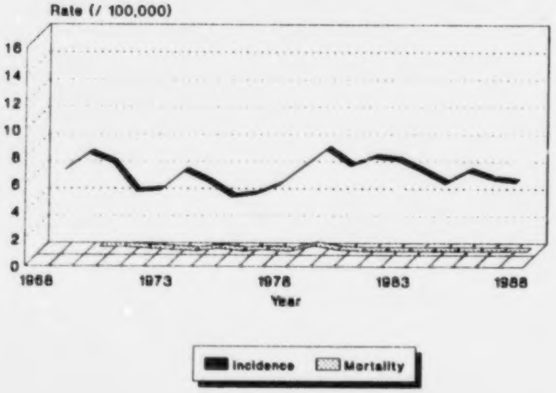
Males



Females

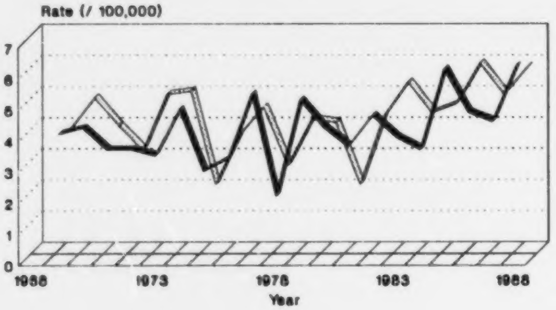


Total Population

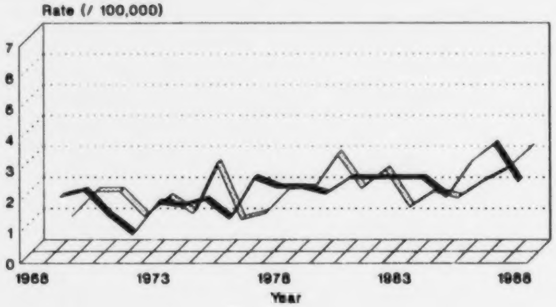


20-YEAR TRENDS
Oesophagus

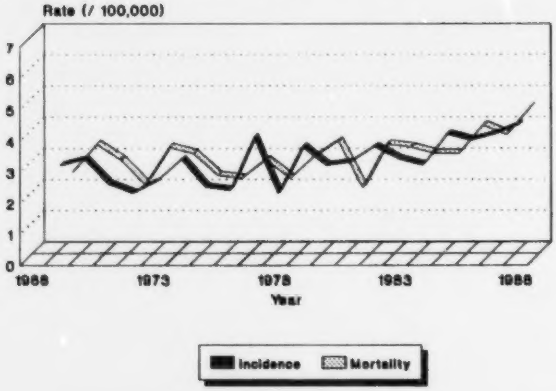
Males



Females



Total Population

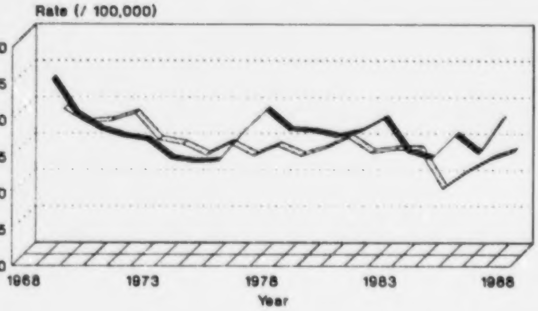


■ Incidence ▨ Mortality

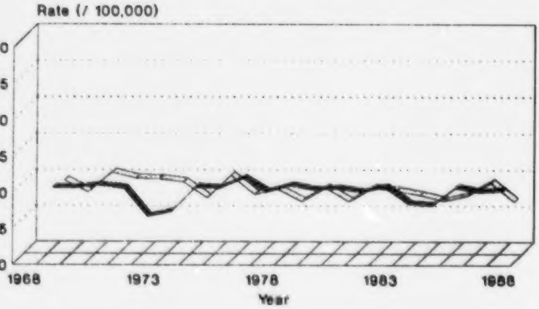
20-YEAR TRENDS

Stomach

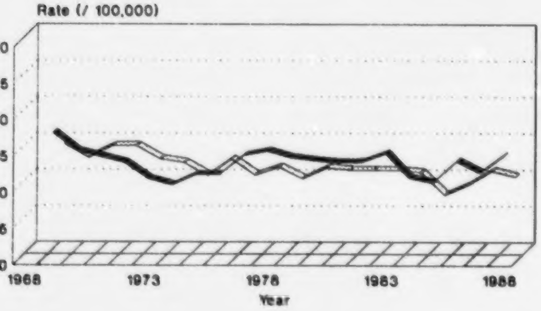
Males



Females



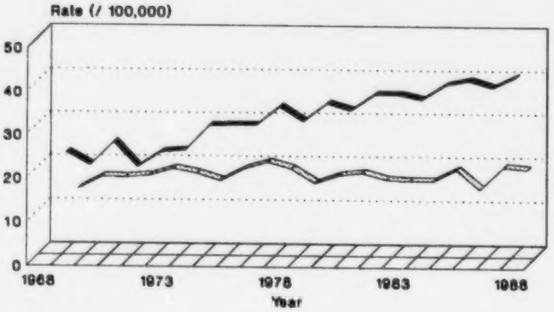
Total Population



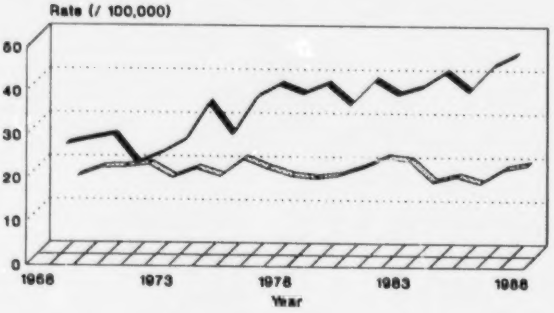
■ Incidence ▨ Mortality

20-YEAR TRENDS
Large Bowel

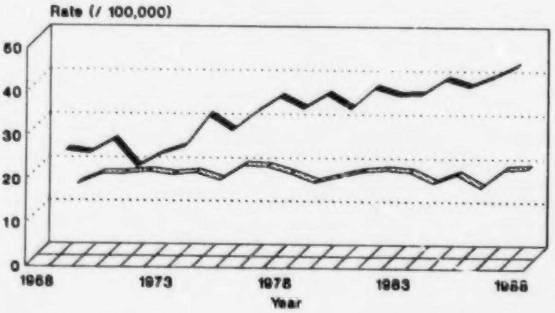
Males



Females



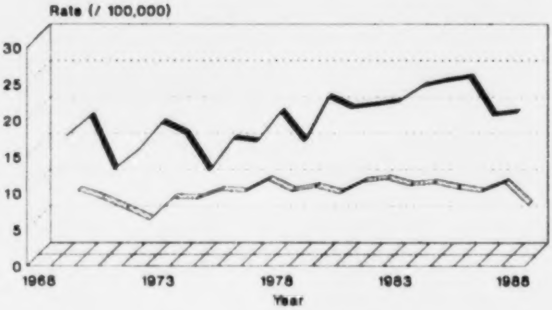
Total Population



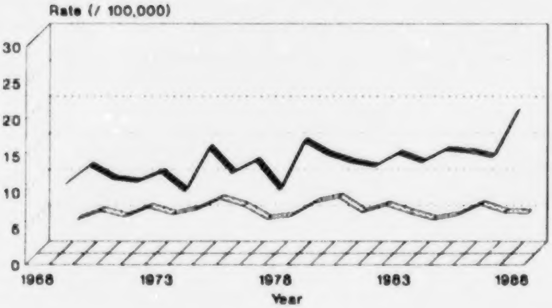
■ Incidence ▨ Mortality

20-YEAR TRENDS
Rectum

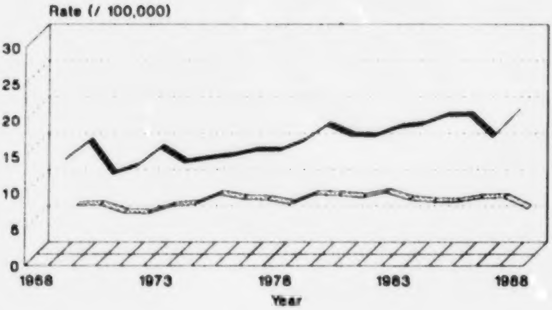
Males



Females



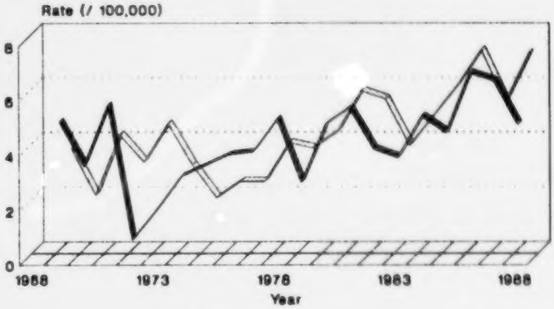
Total Population



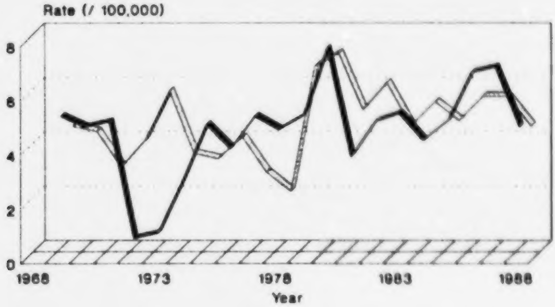
■ Incidence ▨ Mortality

20-YEAR TRENDS
Liver

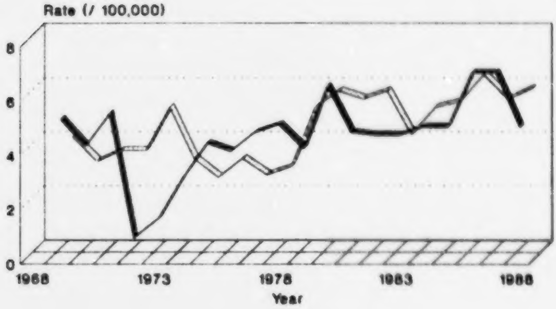
Males



Females



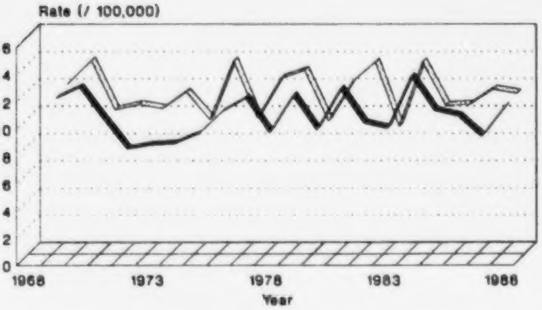
Total Population



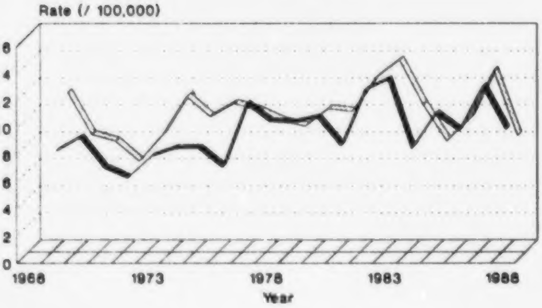
■ Incidence ▨ Mortality

20-YEAR TRENDS
Pancreas

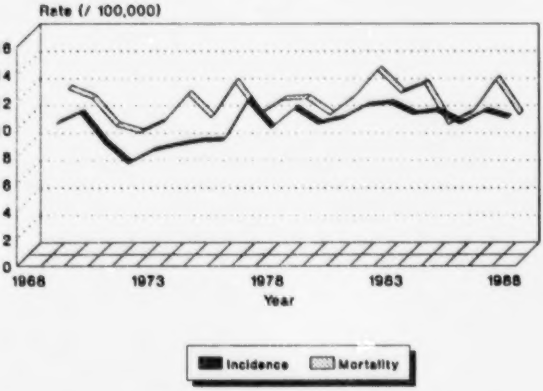
Males



Females

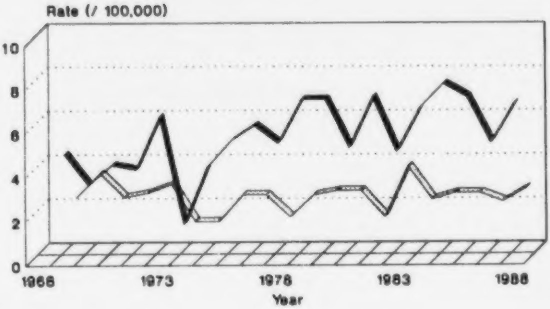


Total Population

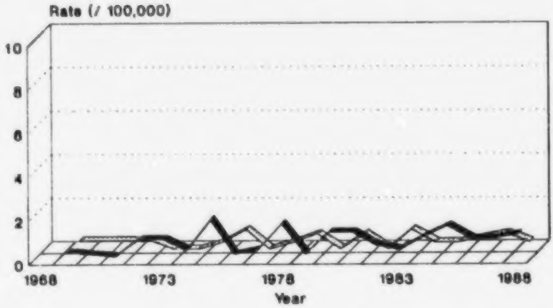


20-YEAR TRENDS
Larynx

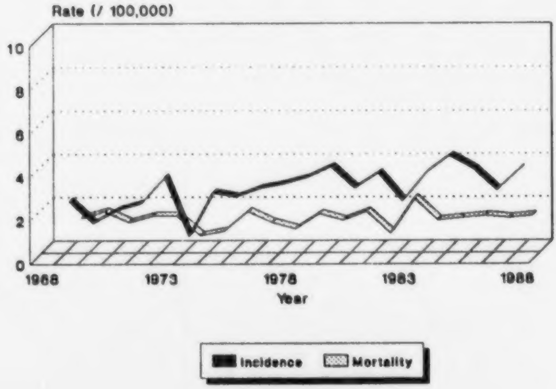
Males



Females

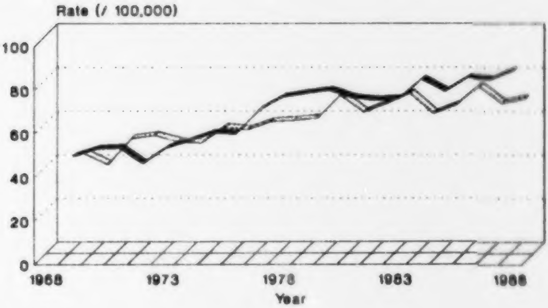


Total Population

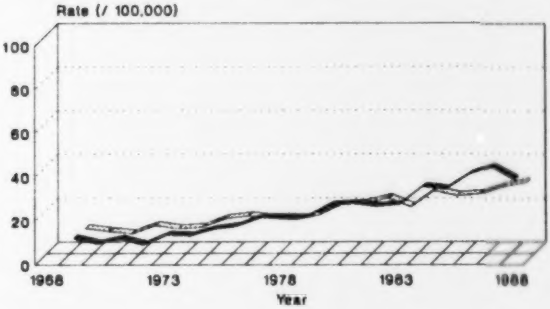


20-YEAR TRENDS
Trachea, Bronchus & Lung

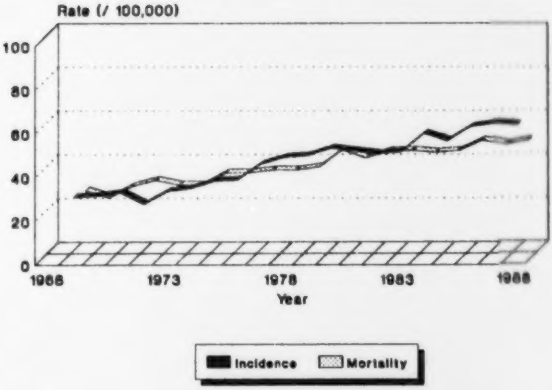
Males



Females

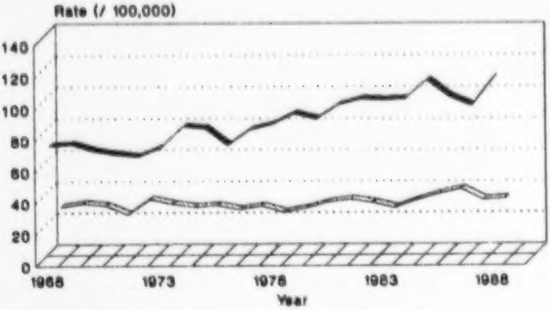


Total Population



20-YEAR TRENDS
Breast

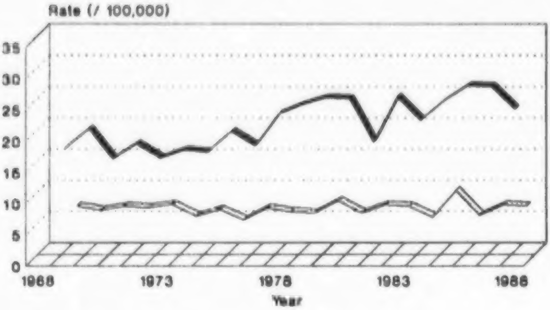
Females



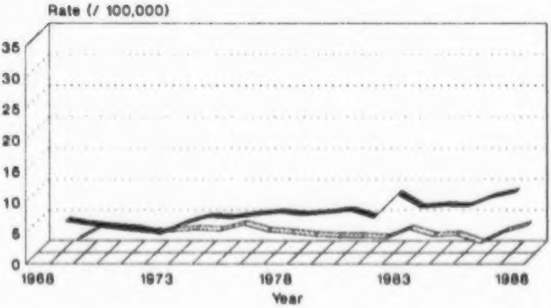
■ Incidence ▨ Mortality

20-YEAR TRENDS
Bladder

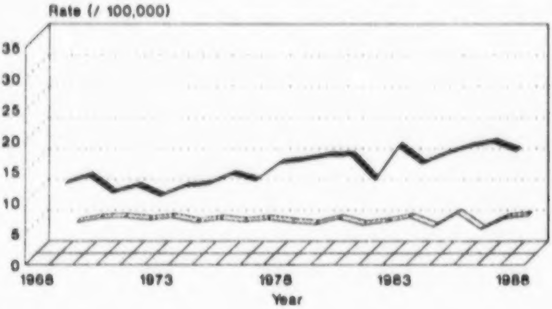
Males



Females



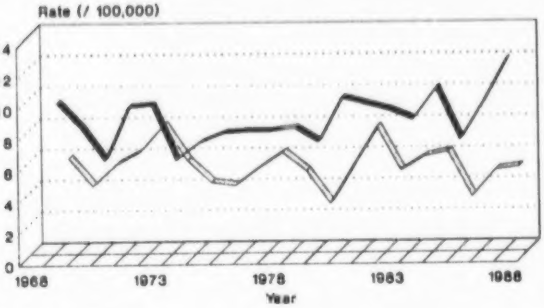
Total Population



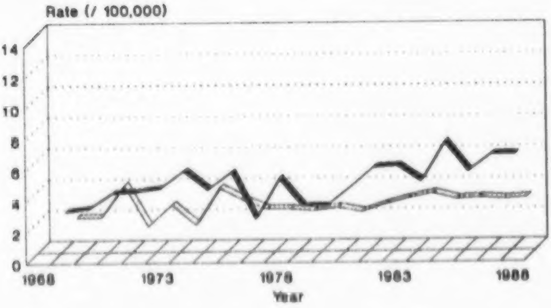
■ Incidence ▨ Mortality

20-YEAR TRENDS
Kidney

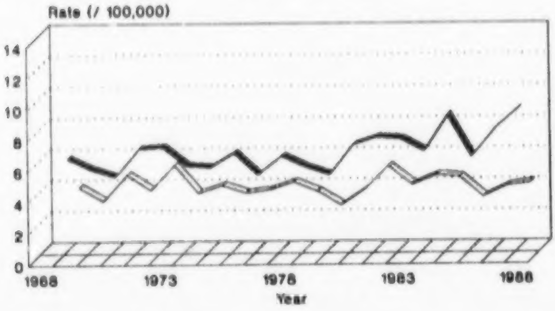
Males



Females



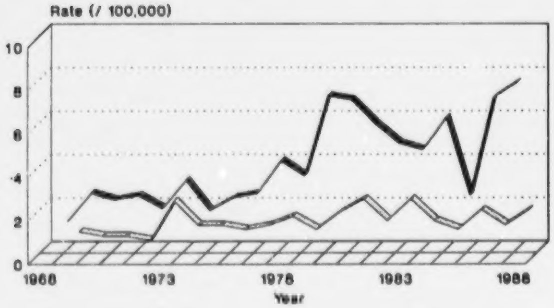
Total Population



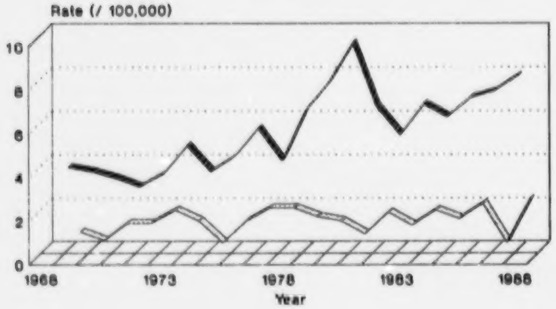
■ Incidence ▨ Mortality

20-YEAR TRENDS
Melanoma

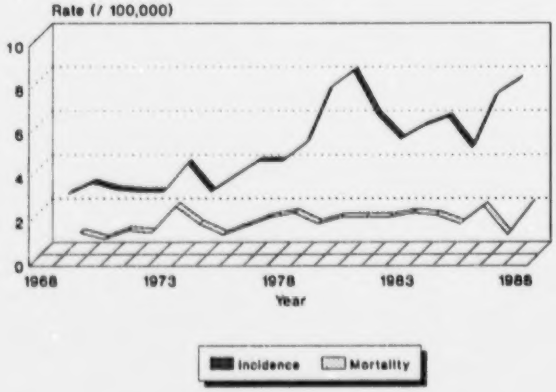
Males



Females

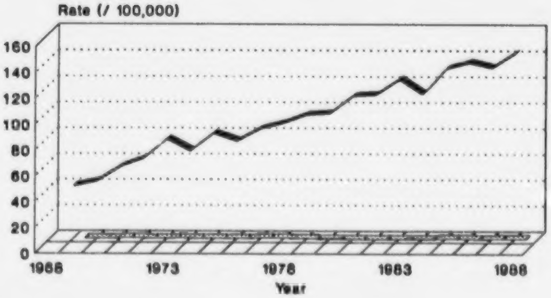


Total Population

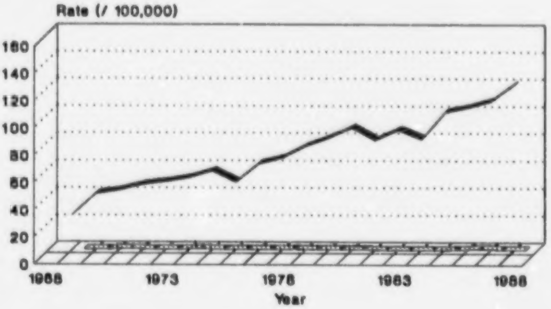


20-YEAR TRENDS
Other Malignant Neoplasms
Skin:

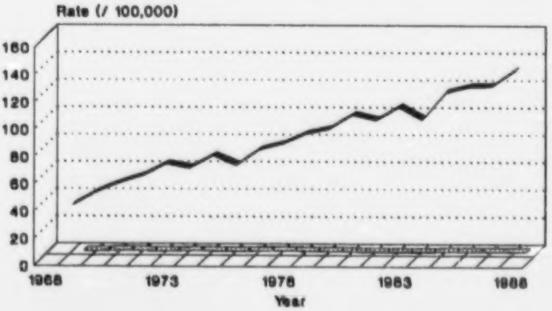
Males



Females



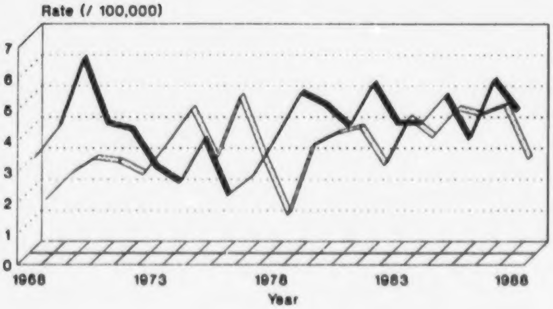
Total Population



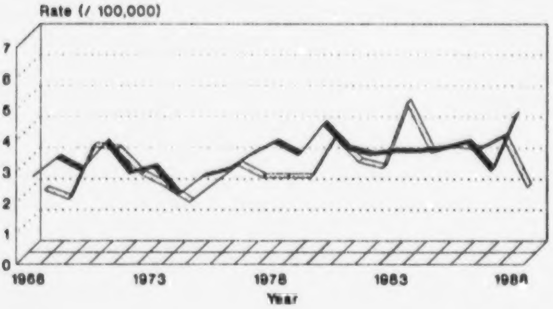
■ Incidence ▨ Mortality

20-YEAR TRENDS
Multiple Myeloma

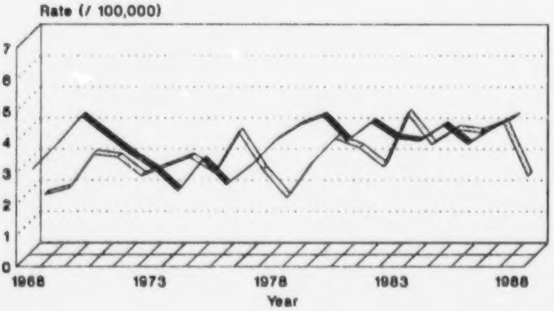
Males



Females



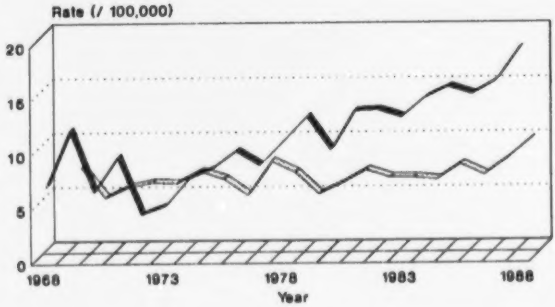
Total Population



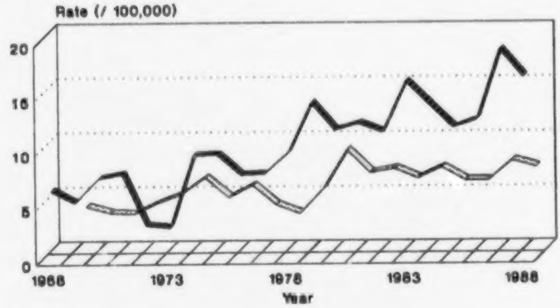
■ Incidence ▨ Mortality

20-YEAR TRENDS
Lymphomas

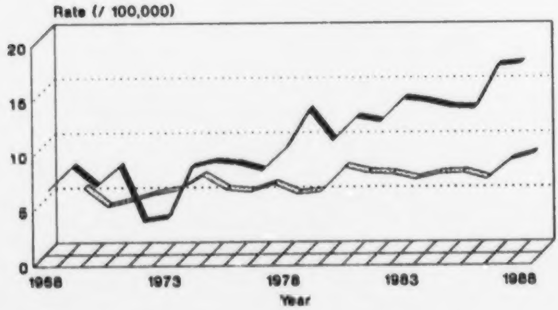
Males



Females



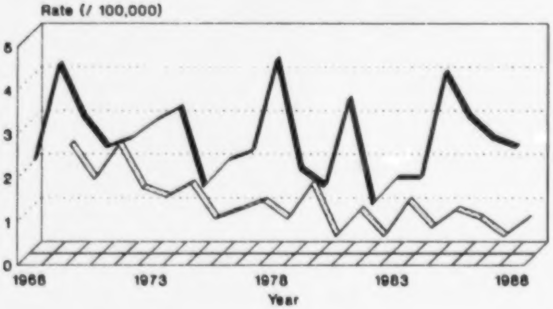
Total Population



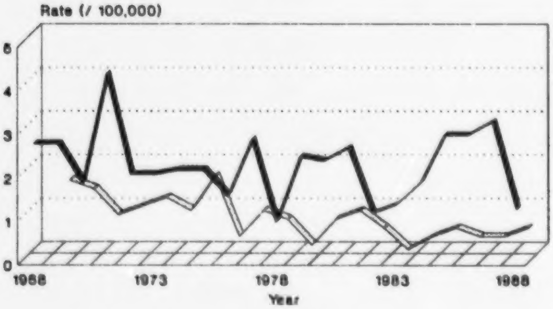
▇ Incidence ▨ Mortality

20-YEAR TRENDS
Hodgkins Disease

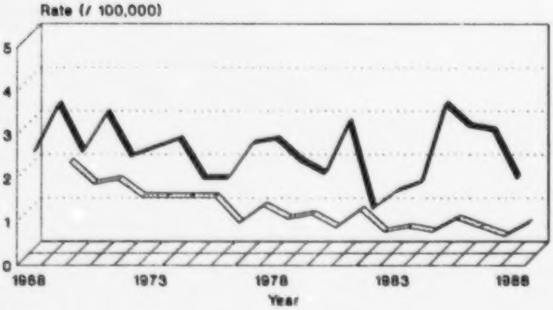
Males



Females



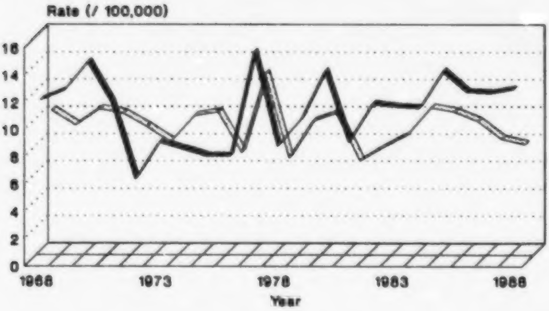
Total Population



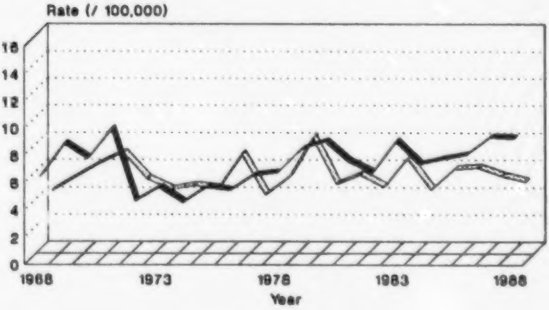
■ Incidence ☐ Mortality

20-YEAR TRENDS
Leukaemia

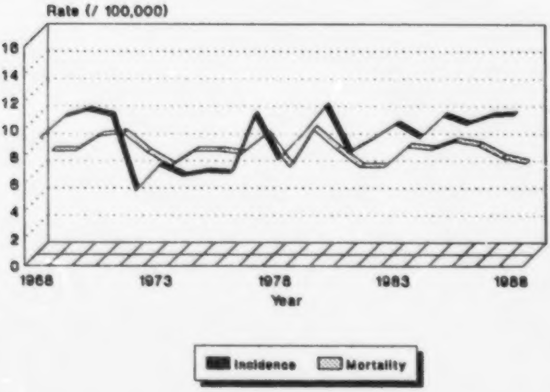
Males



Females

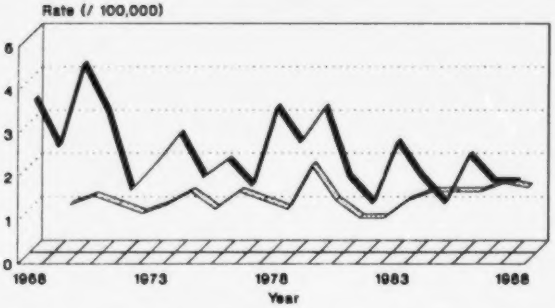


Total Population

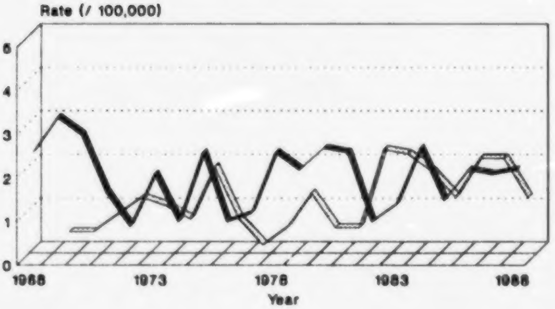


20-YEAR TRENDS
Connective Tissue

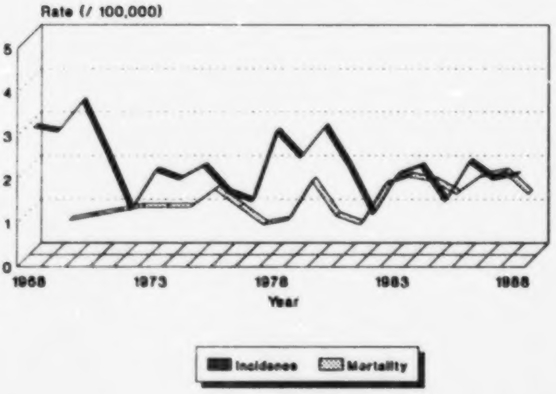
Males



Females

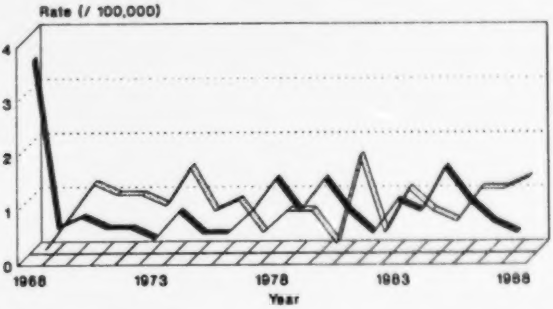


Total Population

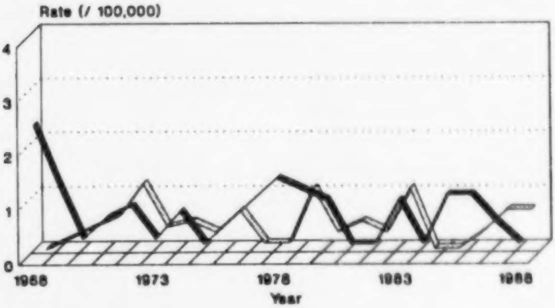


20-YEAR TRENDS
Bone

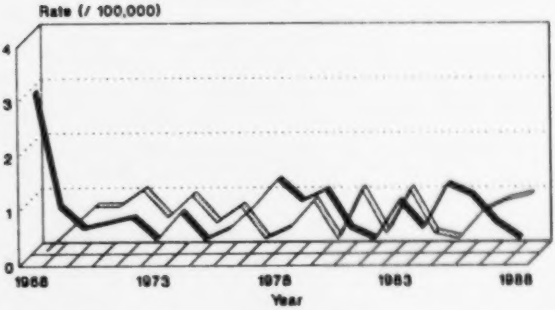
Males



Females



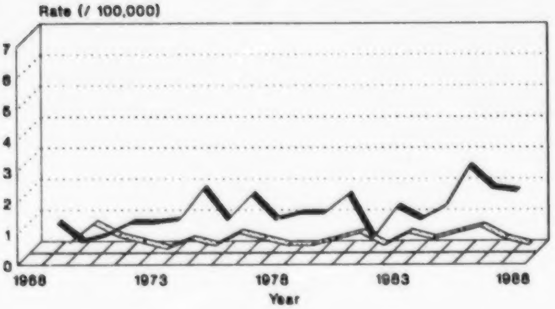
Total Population



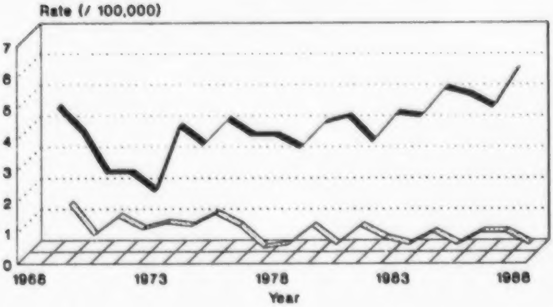
■ Incidence ▨ Mortality

20-YEAR TRENDS
Thyroid

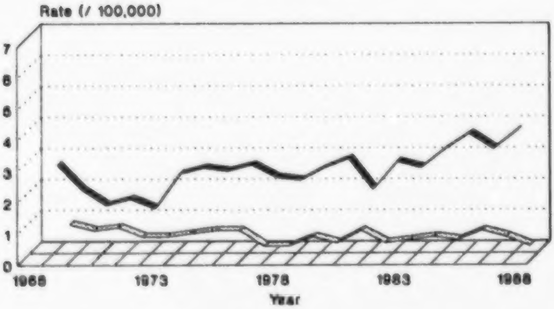
Males



Females



Total Population

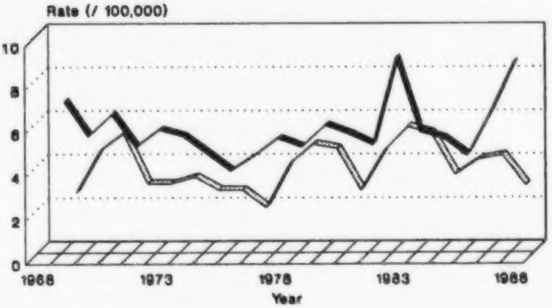


▇ Incidence ▨ Mortality

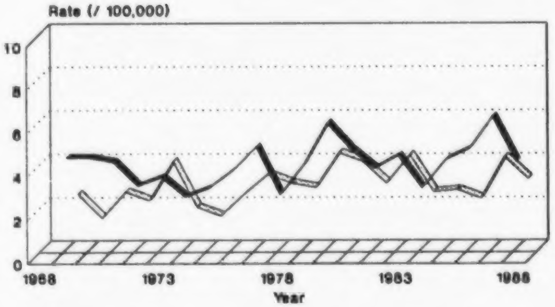
20-YEAR TRENDS

Brain

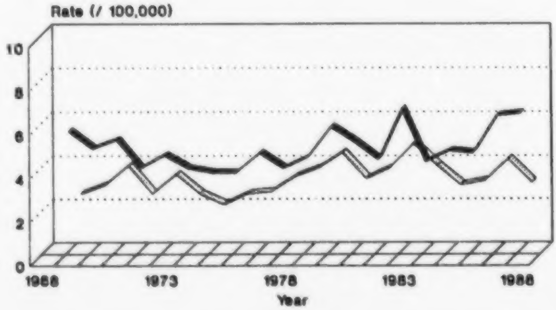
Males



Females



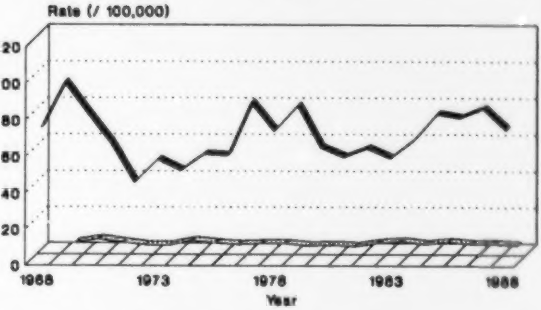
Total Population



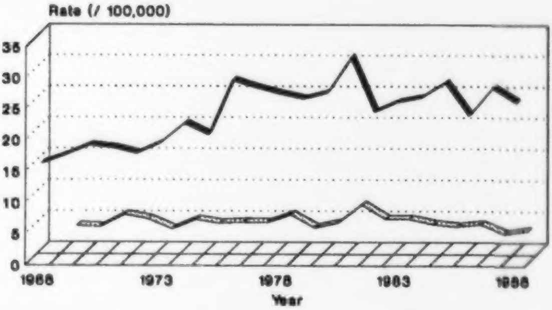
■ Incidence ▨ Mortality

20-YEAR TRENDS

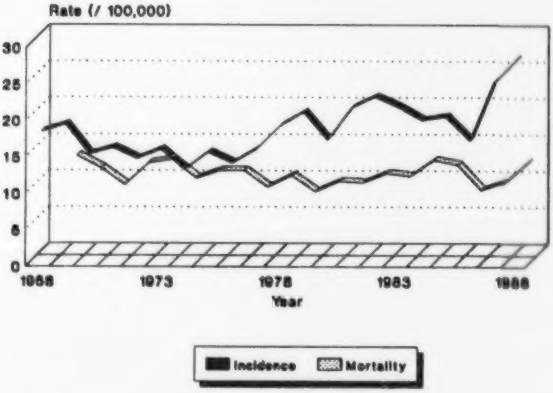
Cervix

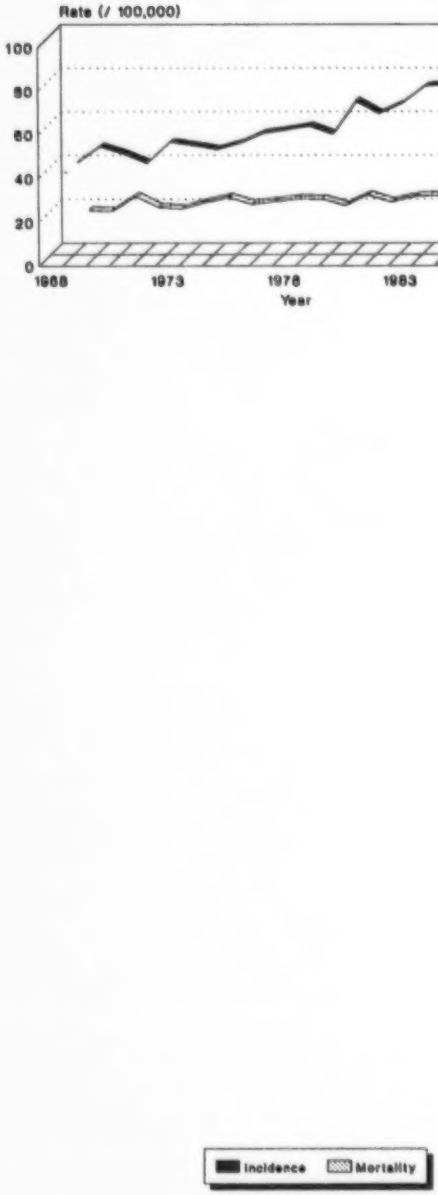


Uterus



Ovary



20-YEAR TRENDS
Prostate